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=> fil reg; d que 14
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STRUCTURE FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1
 DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

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REGISTRY includes numerically searchable data for experimental and
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<http://www.cas.org/support/stngen/stdoc/properties.html>

L4 2 SEA FILE=REGISTRY ABB=ON "L-VALINAMIDE, N,O,B,B-TETR
 AMETHYL-L-TYROSYL-N-((1S,2E)-3-CARBOXY-1-(1-METHYLETHYL)-2-BUTE
 NYL)-N,3-DIMETHYL"?/CN

=> fil capl; d que nos 150
 FILE 'CAPLUS' ENTERED AT 12:33:52 ON 08 SEP 2008
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FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11
 FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

Caplus now includes complete International Patent Classification (IPC)
 reclassification data for the second quarter of 2008.

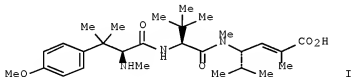
Effective October 17, 2005, revised CAS Information Use Policies apply.
 They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L4 2 SEA FILE=REGISTRY ABB=ON "L-VALINAMIDE, N,O,B,B-TETR
AMETHYL-L-TYROSYL-N-((1S,2E)-3-CARBOXY-1-(1-METHYLETHYL)-2-BUTE
NYL)-N,3-DIMETHYL"?/CN
L50 2 SEA FILE=CAPLUS ABB=ON L4

```
=> d ibib abs hitstr 150
```

150 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:617803 CAPLUS Full-text
 DOCUMENT NUMBER: 141:314607
 TITLE: Synthesis and Biological Activity of Analogues of the
 Antimicrotubule Agent N, β , β -Trimethyl-L-
 phenylalanyl-N1-[(1S,2E)-3-carboxy-1-isopropylbut-2-
 enyl]-L1,3-dimethyl-L-valinamide (HTI-286)
 AUTHOR(S): Zask, Arie; Birnberg, Gary; Cheung, Katherine; Kaplan,
 Joshua; Niu, Chuan; Norton, Emily; Suayan, Ronald;
 Yamashita, Ayako; Cole, Derek; Tang, Zhilian;
 Krishnamurthy, Girija; Williamson, Robert; Khafizova,
 Gulnaz; Musto, Sylvia; Hernandez, Richard; Annable,
 Tami; Yang, Xiaoran; Discafani, Carolyn; Beyer, Carl;
 Greenberger, Lee M.; Loganzo, Frank; Ayral-Kaloustian,
 Semiramis
 CORPORATE SOURCE: Chemical and Screening Sciences, and Oncology
 Research, Wyeth Research, Pearl River, NY, 10965, USA
 SOURCE: Journal of Medicinal Chemistry (2004), 47(19),
 4774-4786
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:314607
 GI



AB Hemiasterlin, a ripeptide isolated from marine sponges, induces microtubule depolymn. and mitotic arrest in cells. HTI-286, an analog from an initial study of the hemiasterlins, is presently in clin. trials. In addition to its potent antitumor effects, HTI-286 has the advantage of circumventing the P-glycoprotein-mediated resistance that hampers the efficacy of other antimicrotubule agents such as paclitaxel and vincristine in animal models. This paper describes an in-depth study of the structure-activity relationships (SAR) of analogs of HTI-286, their effects on microtubule polymerization, and their in vitro and in vivo anticancer activity. Regions of the mol. necessary for potent activity are identified. Groups tolerant of modification, leading

to novel analogs, are reported. Potent analogs identified through in vivo studies in tumor xenograft models include one superior analog, HTI-042 (I).

IT 676633-19-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of analogs of peptide HTI-286 and SAR study of their anticancer activity and effects on microtubule polymerization)

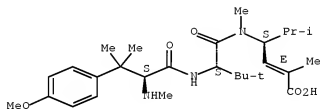
RN 676633-19-5 CAPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 676633-18-4
 CMF C28 H45 N3 O5

Absolute stereochemistry.
 Double bond geometry as shown.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 150 2

L50 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:267231 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 140:304081
 TITLE: Preparation of peptides for treating resistant tumors
 INVENTOR(S): Greenberger, Lee Martin; Loganzo, Frank, Jr.;
 Discafani-Marro, Carolyn Mary; Zask, Arie;
 Ayral-Kaloustian, Semiramis
 PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA

SOURCE: PCT Int. Appl., 442 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026293	A2	20040401	WO 2003-US29832	20030918
WO 2004026293	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2406504	A1	20040320	CA 2002-2406504	20021003
AU 2003275126	A1	20040408	AU 2003-275126	20030918
US 20040121965	A1	20040624	US 2003-666722	20030918
PRIORITY APPLN. INFO.:			US 2002-411883P	P 20020920
			WO 2003-US29832	W 20030918

OTHER SOURCE(S): MARPAT 140:304081

AB The invention provides peptides R1R2NCH(CR3R4R5)CONR6CHR7CONR8R9 [R1-R8 are H or an (un)saturated moiety having a linear, branched, or cyclic skeleton containing 1-10 (un)substituted carbon atoms and 0-4 each nitrogen, oxygen, or sulfur atoms; or R1R2N or R3R4C is a 3- to 7-membered ring; R9 is -Y-CO-Z, where Y is alkyl and Z is OH, SH, NH2, an amino acid residue, etc. (with provisos)] for treating or inhibiting the growth or eradication of tumors which are resistant to at least one chemotherapeutic agent. Thus, N, β , β -trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and shown to be a potent inhibitor of cell growth in 34 tumor cell lines (mean IC50 = 2.1 \pm 1.7 nM, median 1.7 nM, range 0.2-7.3 nM) and is distinct from paclitaxel which has an usually large range of activity. The activity is independent of tumor origin and in many cases this peptide is considerably more potent than paclitaxel.

IT 676633-18-4P 676633-19-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

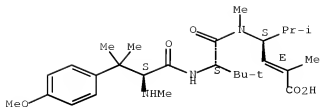
(preparation of peptides for treating resistant tumors)

RN 676633-18-4 CAPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 676633-19-5 CAPLUS

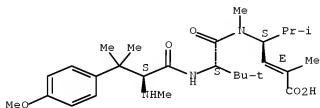
CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

CM 1

CRN 676633-18-4

CMF C28 H45 N3 O5

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



STRUCTURES FOR COMPOUNDS OF CLAIM 3

=> fil reg; d ide 148 1-5
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 DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
 predicted properties as well as tags indicating availability of
 experimental property data in the original document. For information
 on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

L48 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN

RN 114977-28-5 REGISTRY

ED Entered STN: 25 Jun 1988

CN Benzenepropanoic acid, β -[[[(1,1-dimethylethoxy)carbonyl]amino]-
 α -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-
 (benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-
 trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-
 cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (α R, β S)- (CA INDEX
 NAME)

OTHER CA INDEX NAMES:

CN 7,11-Methano-1H-cyclodeca[3,4]benz[1,2-b]oxete, benzenepropanoic acid
 deriv.

CN Benzenepropanoic acid, β -[[[(1,1-dimethylethoxy)carbonyl]amino]-
 α -hydroxy-, 12b-(acetyloxy)-12-(benzoyloxy)-
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
 ester, [2aR-[2a α ,4 β ,4a β ,6 β ,9 α (α R*, β S
 *),11 α ,12 α ,12a α ,12b α]]-

OTHER NAMES:

CN Docetaxel

CN Docetaxol

CN N-Debenzoyl-N-tert-butoxycarbonyl-10-deacetyltaxol

CN RP 56976

CN Taxotere

FS STEREOSEARCH

DR 216252-50-5

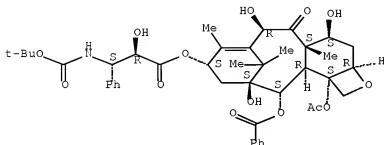
MF C43 H53 N O14

CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IMSCSEARCH, IMSDRUGNEWS, IMPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5044 REFERENCES IN FILE CA (1907 TO DATE)
 170 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 5071 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L48 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN

RN 71486-22-1 REGISTRY

ED Entered STN: 16 Nov 1984

CN Aspidospermidine-3-carboxylic acid, 4-(acetyloxy)-6,7-didehydro-15-[(2R,6R,8S)-4-ethyl-1,3,6,7,8,9-hexahydro-8-(methoxycarbonyl)-2,6-methano-2H-azecino[4,3-b]indol-8-yl]-3-hydroxy-16-methoxy-1-methyl-, methyl ester, (2β,3β,4β,5α,12R,19α)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN C'-Norvincal leukoblastine, 3',4'-didehydro-4'-deoxy-

OTHER NAMES:

CN Aspidospermidine-3-carboxylic acid, 4-(acetyloxy)-6,7-didehydro-15-[(2R,6R,8S)-4-ethyl-1,3,6,7,8,9-hexahydro-8-(methoxycarbonyl)-2,6-methano-2H-azecino[4,3-b]indol-8-yl]-3-hydroxy-16-methoxy-1-methyl-, methyl ester, (2β,3β,4β,5α,12β,19α)-

CN F 80520

CN KW 2307 base

CN Navelbin

CN Navelbine base

CN Nor-5'-anhydrovinblastine

CN Vinorelbine

FS STEREOSEARCH

MF C45 H54 N4 O8

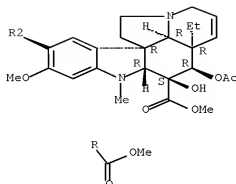
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)

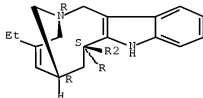
Other Sources: WHO

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1894 REFERENCES IN FILE CA (1907 TO DATE)

42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1907 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L48 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN

RN 33969-62-4 REGISTRY

ED Entered STN: 16 Nov 1984

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-,
 (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-
 2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl
 ester, (α R, β S)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 7, 11-Methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxete, benzenepropanoic acid
 deriv.

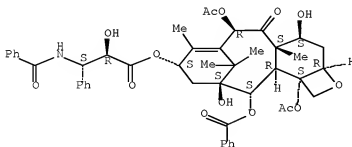
CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-,
 6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-
 dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-
 cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, [2aR-
 [2aa, 4 β , 4a β , 6 β , 9a(α R*, β S*)], 11a
 , 12a, 12aa, 12ba]]-

CN Tax-11-en-9-one, 5 β ,20-epoxy-1,2 α ,4,7 β ,10 β ,13 α -
hexahydroxy-, 4,10-diacetate 2-benzoate 13-ester with (2R,3S)-N-benzoyl-3-
phenylisoserine (8CI)

OTHER NAMES:

CN ABI 007
CN Abraxane
CN BMS 181339-01
CN Capzol
CN DHP 107
CN Ebetaxel
CN EndoTAG 1
CN Genaxol
CN Genetaxyl
CN Genexol
CN Genexol-PM
CN MBT 0206
CN Mitotax
CN NK 105
CN NSC 125973
CN OncoGel
CN Onxal
CN Pacliex
CN Paclitaxel
CN Plaxicel
CN QW 8184
CN TaxAlbin
CN Taxol
CN Taxol A
CN Yewtaxan
FS STEREOSEARCH
DR 157069-30-2
MF C47 H51 N O14
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST,
CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, HSDB*, IFICDB, IFIUDB,
IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA,
MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PHAR, PIRA, PROMT, PROUSDDR, PS,
RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).

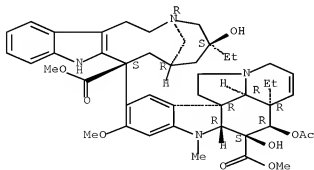


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15676 REFERENCES IN FILE CA (1907 TO DATE)
 767 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 15740 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L48 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
 RN 865-21-4 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN Vincal leukoblastine (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 1H-Indolizino[8,1-cd]carbazole, vincal leukoblastine deriv.
 CN 2H-3,7-Methanoazacycloundecino[5,4-b]indole, vincal leukoblastine deriv.
 CN Vinblastine (7CI)
 OTHER NAMES:
 CN (+)-Vinblastine
 CN 1H-Indolizino[8,1-cd]carbazole-5-carboxylic acid, 4-(acetyloxy)-3a-ethyl-9-[5-ethyl-1,4,5,6,7,8,9,10-octahydro-5-hydroxy-9-(methoxycarbonyl)-2H-3,7-methanoazacycloundecino[5,4-b]indol-9-yl]-3a,4,5,5a,6,11,12,13a-octahydro-5-hydroxy-8-methoxy-6-methyl-, methyl ester, [3aR-[3aα,4β,5β,5aβ,9(3R*,5S*,7R*,9S*),10bR*,13aα]]-
 CN Rozevin
 CN Valban
 CN Vinblastin
 CN Vincal eucoblastin
 CN Vincal eucoblastine
 CN VLB
 CN [3aR-[3aα,4β,5β,5aβ,9(3R*,5S*,7R*,9S*),10bR*,13a.α.a.]]-Methyl 4-(acetyloxy)-3a-ethyl-9-[5-ethyl-1,4,5,6,7,8,9,10-octahydro-5-hydroxy-9-(methoxycarbonyl)-2H-3,7-methanoazacycloundecino[5,4-b]indol-9-yl]-3a,4,5,5a,6,11,12,13a-octahydro-5-hydroxy-8-methoxy-6-methyl-1H-indolizino[8,1-cd]carbazole-5-carboxylate
 FS STEREOSEARCH
 DR 7060-58-4, 57-23-8
 MF C46 H58 N4 O9
 CI COM
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6109 REFERENCES IN FILE CA (1907 TO DATE)
 221 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 6125 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L48 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN

RN 57-22-7 REGISTRY

ED Entered STN: 16 Nov 1984

CN Vincal leukoblastine, 22-oxo- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indolizino[8,1-cd]carbazole, vincal leukoblastine deriv.

CN 2H-3,7-Methanoazacycloundecino[5,4-b]indole, vincal leukoblastine deriv.

CN Leurocristine (7CI, 8CI)

OTHER NAMES:

CN (+)-Vincristine

CN 22-Oxovin cal leukoblastine

CN LCR

CN Leucristine

CN OncoTCS

CN VCR

CN Vincristin

CN Vincristine

CN Vinkristin

FS STEREOSEARCH

DR 28379-27-3

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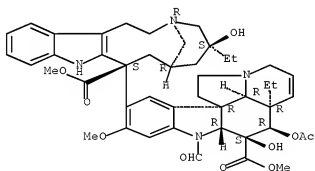
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PROMT, PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD, VETU
 (*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8117 REFERENCES IN FILE CA (1907 TO DATE)

176 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

8144 REFERENCES IN FILE CAPLUS (1907 TO DATE)

8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

SEARCH OF CLAIM 1

=> fil reg; d stat que l41
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STRUCTURE FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1
 DICTIONARY FILE UPDATES: 7 SEP 2008 HIGHEST RN 1047406-12-1

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

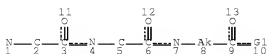
Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
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 experimental property data in the original document. For information
 on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

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VAR G1=O/S/N

NODE ATTRIBUTES:

NSPEC IS RC AT 1
 NSPEC IS RC AT 2
 CONNECT IS E3 RC AT 5
 DEFAULT MLEVEL IS ATOM
 DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 13031 ITERATIONS
 SEARCH TIME: 00.00.02

11974 ANSWERS

=> fil capl; d que nos 160; d que nos 164; d que nos 166
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FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11
 FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>
 'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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=> d que nos 174

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L42     PRD<20020920)
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L80 ANSWER 1 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1321643 CAPLUS Full=Text
DOCUMENT NUMBER: 145:116381
TITLE: HTI-286, a synthetic analog of the antimitotic natural
product hemiasterlin
AUTHOR(S): Andersen, Raymond J.; Roberge, Michel
CORPORATE SOURCE: Dept of Chemistry, University of British Columbia,
Vancouver, BC, V6T 1Z1, Can.
SOURCE: Anticancer Agents from Natural Products (2005),
267-280. Editor(s): Cragg, Gordon M.; Kingston, David
G. I.; Newman, David J. CRC Press LLC: Boca Raton,
Fla.
CODEN: 69HQYQ; ISBN: 0-8493-1863-7
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review. HTI-286 is a synthetic exptl. anticancer drug currently in phase II
clin. trials for the treatment of non-small lung cancer. It shows activity in
a wide variety of tumor xenograft models, including several multidrug-
resistant tumors. The lead structure for the development of HTI-286 was the

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sponge tripeptide hemiasterlin, a microtubule depolymerizing agent that kills cells by causing mitotic arrest, leading to apoptosis. The sequence of discoveries that led to the development of HTI-286 and a profile of its biological activities are described.

CC 1-0 (Pharmacology)

IT Antitumor agents

(antimitotic agent HTI-286 targeted tubulin inhibiting its polymerization

into

microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT Structure-activity relationship

(antitumor; anticancer agent HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT Drug resistance

Human

Microtubule

(hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT Tubulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT Apoptosis

(microtubule depolymerizing agent HTI-286 killed cells by mitotic arrest thereby lead to apoptosis in mouse xenograft model)

IT Drug toxicity

(phase I trial identified dose limiting toxicity and maximum tolerated dose of HTI-286 which target tubulin and inhibit its polymerization into microtubule and showed activity against multidrug-resistant human tumors in mouse xenograft model)

IT 157207-90-4, Hemiasterlin

RL: BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT 228266-40-8, HTI-286

RL: PAC (Pharmacological activity); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

IT 157207-90-4, Hemiasterlin

RL: BSU (Biological study, unclassified); THU (Therapeutic use);

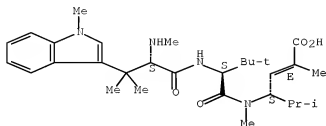
BIOL (Biological study); USES (Uses)

(hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)

RN 157207-90-4 CAPLUS

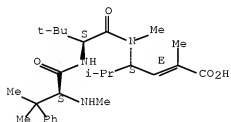
CN L-Valinamide, N,β,β,1-tetramethyl-L-tryptophyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-buten-1-yl]-N,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 228266-40-8, HTI-286
 RL: PAC (Pharmacological activity); PRP (Properties); THO (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hemiasterlin analog HTI-286 targeted tubulin inhibiting its polymerization into microtubules, also showed activity against drug-sensitive and multidrug-resistant human tumor in mouse xenograft model)
 RN 228266-40-8 CAPLUS
 CN L-Valinamide, N,β,β-trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-buten-1-yl]-N,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 2 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:563126 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 143:108821
 TITLE: Taltobulin: oncolytic drug tubulin polymerization inhibitor antimetabolic drug
 AUTHOR(S): Ayral-Kaloustian, S.; Zask, A.
 CORPORATE SOURCE: Wyeth Research, Pearl River, NY, 10965, USA
 SOURCE: Drugs of the Future (2005), 30(3), 254-260
 CODEN: DRFUD4; ISSN: 0377-8282
 PUBLISHER: Prous Science
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Antimicrotubule agents are among the most effective drugs for the treatment of breast, ovarian and other forms of cancer. Two classes of antimicrotubule drugs are commonly used: the taxanes, which accelerate tubulin polymerization by stabilizing assembled microtubules and obstructing

depolymer., and the Vinca alkaloids, which bind to the tubulin α/β -heterodimer, block the formation of normal microtubules and lead to the depolymer. of microtubules and/or the formation of abnormal tubulin polymers. While these drugs inhibit tumor progression, their cytotoxic effects on rapidly proliferating normal tissues and other significant side effects are limiting factors. In addition, inherent resistance to antimicrotubule agents is encountered in many tumor types, or acquired resistance may occur during multiple cycles of therapy. Thus, there is great interest in and an unmet need for identifying novel antimicrotubule drugs. Taltobulin (HTI-286, SPA-110) is a novel antimitotic agent that inhibits the polymerization of tubulin, disrupts microtubule dynamics in cells and induces mitotic arrest and apoptosis. Relative to the antimicrotubule drugs in use, taltobulin exhibits significantly less interaction with the multidrug resistance protein (P-glycoprotein) and is effective in inhibiting human tumor xenografts in nude mouse models where paclitaxel and vincristine are ineffective. Taltobulin administered i.v. or p.o. in saline inhibits the growth of numerous human tumors without the side effects associated with formulations. Taltobulin is in clin. development.

CC 1-0 (Pharmacology)

IT Antitumor agents
(antitumor agent taltobulin inhibits polymerization of tubulin, disrupts microtubule dynamics in cell and induces mitotic arrest and apoptosis in human tumor xenograft in mouse)

IT P-glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(taltobulin effective in inhibiting human tumor xenograft in mouse and shows less interaction with multidrug resistance P-glycoprotein)

IT Human Mitosis
(taltobulin inhibits polymerization of tubulin, disrupts microtubule dynamics in cell and induces mitotic arrest and apoptosis in human tumor xenograft in mouse)

IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tubulin polymerization inhibitor taltobulin inhibits polymerization of

tubulin,
disrupts microtubule dynamics in cell and induces mitotic arrest and apoptosis in human tumor xenograft in mouse)

IT 228266-40-8, Taltobulin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(taltobulin inhibits polymerization of tubulin, disrupts microtubule dynamics in cell and induces mitotic arrest and apoptosis in human tumor xenograft in mouse)

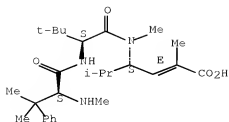
IT 228266-40-8, Taltobulin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(taltobulin inhibits polymerization of tubulin, disrupts microtubule dynamics in cell and induces mitotic arrest and apoptosis in human tumor xenograft in mouse)

RN 228266-40-8 CAPLUS

CN L-Valinamide, N, β , β -trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-buten-1-yl]-N,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 3 OF 52 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2005:220117 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291898
 TITLE: Peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof
 INVENTOR(S): Siler-Khodro, Theresa M.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 90 pp., Cont.-in-part of U.S. Ser. No. 639,405.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050054576	A1	20050310	US 2004-820477	20040408
US 20040152639	A1	20040805	US 2003-639405	20030812 <--
EP 1586581	A2	20051019	EP 2005-7788	20050408
EP 1586581	A3	20051221		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

PRIORITY APPLN. INFO.: US 2003-639405 A2 20030812
 US 2001-941094 A2 20010828 <--
 US 2004-820477 A 20040408

AB Chicken II and salmon GnRH or its analog decapeptides resistant to degradation by peptidase incorporating D-arginine, D-leucine, D-tBu-Serine, D-Trp or other active D amino acids at position 6 and ethylamide, aza-Gly-amide or other Gly amide at position 10. The non-mammalian GnRH or its analogs demonstrate preferential binding to male and female reproductive system GnRH receptors as well as tumor cell GnRH receptors in these systems. Biopotency is greater within the reproductive system and at tumor cells than at the pituitary. These non-mammalian GnRH or its analogs may be used in pharmaceutical preps., and specifically in various treatment methods as a contraceptive or post-coital contraceptive agent. The non-mammalian GnRH or its analogs are also provided in pharmaceutical preps. that may be used clin. for maintaining pregnancy when used in very low doses and administered in pulsatile fashion, as well as in preps. for the treatment of male and female reproductive system disorders including cancers of these systems or other system with GnRH II receptors. The aza-Gly (10) amide non-mammalian analogs are yet other embodiments of the non-mammalian GnRH analogs provided as a part of the invention. The claims of this continuation-in-part patent focus on the use of non-mammalian GnRH analogs in treating cancer, methods for determining the

presence of non-mammalian GnRH polypeptides or nucleic acids, and methods of regulating transcription and translation of GnRH polypeptides and GnRH receptors.

- IC ICM A61K038-09
ICS A61K038-24
- INCL 514016000; 530313000
- CC 2-5 (Mammalian Hormones)
- IT Antitumor agents
Cell proliferation
(antibody to chicken GnRH II to regulate cell proliferation; peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT Clupea harengus
Contraceptives
Drug delivery systems
Gallus domesticus
Human
Mammary gland, neoplasm
Neoplasm
Ovary, disease
Reproductive system, disease
Salmon
Shark
Siluriformes
Uterus, disease
(peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT 91097-16-4, Chicken GnRH II
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody to chicken GnRH II to regulate cell proliferation; peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT 9001-92-7, Endoepitidase 53714-56-0, Leuprolide 57982-77-1, Buserelin 72162-84-6, Postproline endoepitidase 112568-12-4, Antide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT 9034-40-6, GnRH 47922-48-5, Chicken GnRH I 91097-16-4D, Chicken GnRH II, analogs 96497-82-4 96513-52-9 101509-61-9, Luteinizing hormone-releasing factor (Squalus acanthias) 144978-60-9, Luteinizing hormone-releasing factor I (Clarias gariepinus) 145940-57-4 335380-72-8 335380-73-9 364728-50-7 847355-04-8 847375-24-0
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT 60556-70-9
RL: PRP (Properties)
(unclaimed sequence; peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)
- IT 91097-16-4, Chicken GnRH II
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

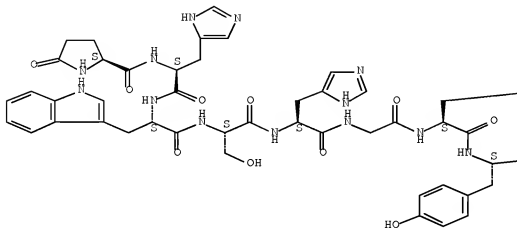
(antibody to chicken GnRH II to regulate cell proliferation; peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)

RN 91097-16-4 CAPLUS

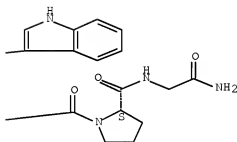
CN Luteinizing hormone-releasing factor II (chicken) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 53714-56-0, Leuprolide 57982-77-1, Buserelin

112569-12-4, Antide

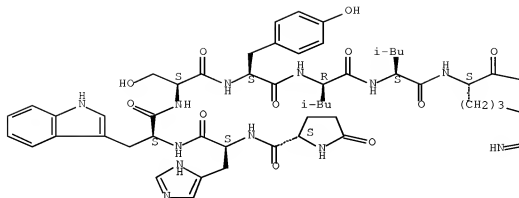
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)

RN 53714-56-0 CAPLUS

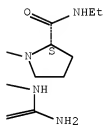
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

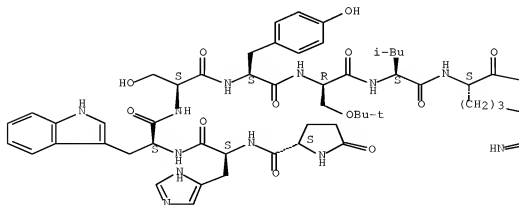


RN 57982-77-1 CAPLUS

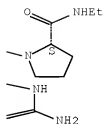
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

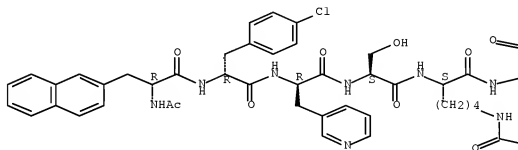


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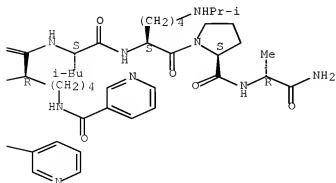
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N6-(3-pyridinylcarbonyl)-L-lysyl-N6-(3-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



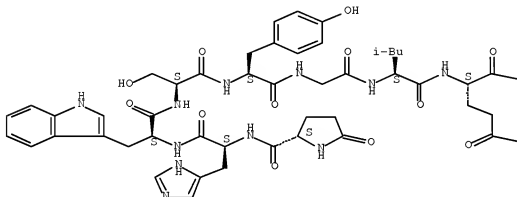
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analogs 96497-82-4 96513-52-9 101599-61-9,
Luteinizing hormone-releasing factor (Squalus acanthias)
144978-60-9, Luteinizing hormone-releasing factor I (Clarias
gariepinus) 145940-57-4 335380-72-8
335380-73-9 364728-50-7 847355-04-8
847375-24-0
RL: BSU (Biological study, unclassified); FAC (Pharmacological
activity); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(peptidase-resistant non-mammalian GnRH analogs and
therapeutic uses thereof)
RN 47922-48-5 CAPLUS
CN Luteinizing hormone-releasing factor I (chicken) (9CI) (CA INDEX NAME)

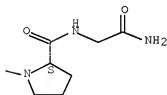
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Absolute stereochemistry.

PAGE 1-A



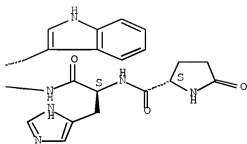
PAGE 1-B

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RN	91097-16-4	CAPLUS			
CN	Luteinizing hormone-releasing factor II (chicken)	(9CI)	(CA INDEX NAME)		

Absolute stereochemistry.

PAGE 1-B

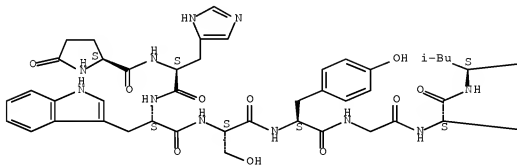


RN 96513-52-9 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 7-L-tryptophan-8-L-leucine-10-glycine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

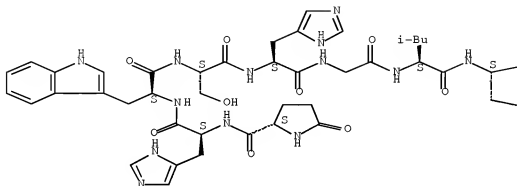


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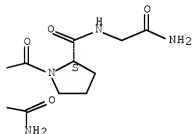
CN Luteinizing hormone-releasing factor I (Clarias gariepinus) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

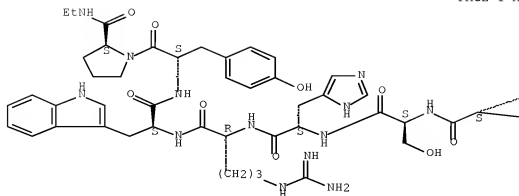


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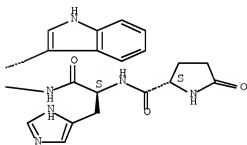
CN L-Prolinamide, 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-histidyl-D-arginyl-L-tryptophyl-L-tyrosyl-N-ethyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

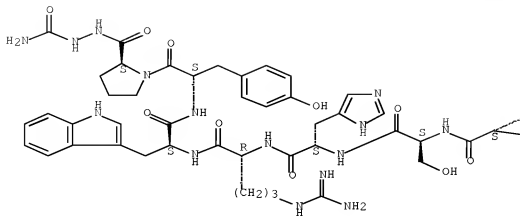


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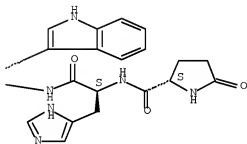
CN L-Proline, 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-histidyl-D-
 arginyl-L-tryptophyl-L-tyrosyl-, 2-(aminocarbonyl)hydrazide (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

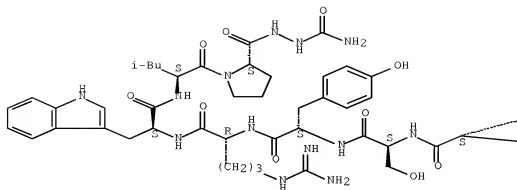


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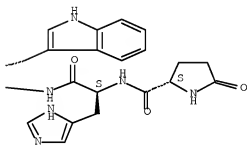
CN L-Proline, 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-
 arginyl-L-tryptophyl-L-leucyl-, 2-(aminocarbonyl)hydrazide (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

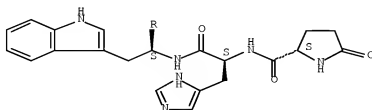


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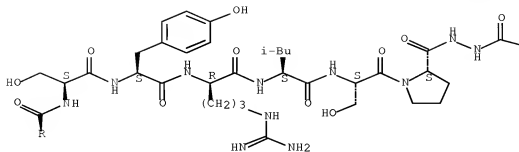
CN L-Proline, 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-
arginyl-L-leucyl-L-seryl-, 2-(aminocarbonyl)hydrazide (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PAGE 2-B

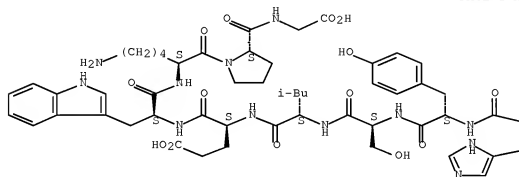
—NH₂

RN 847355-04-8 CAPLUS

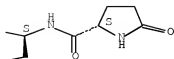
CN Glycine, 5-oxo-L-prolyl-L-histidyl-L-tyrosyl-L-seryl-L-leucyl-L- α -glutamyl-L-tryptophyl-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

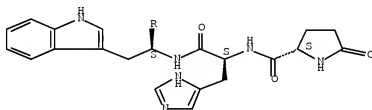


RN 847375-24-0 CAPLUS

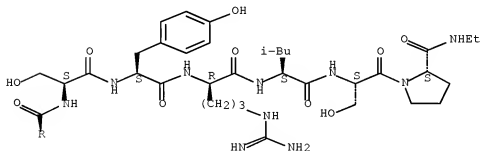
CN L-Prolinamide, 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-arginyl-L-leucyl-L-seryl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 60556-70-9

RL: PRP (Properties)

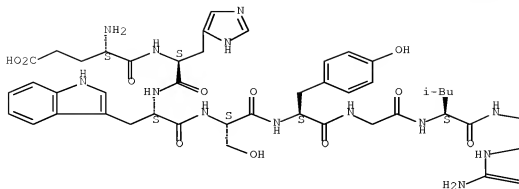
(unclaimed sequence; peptidase-resistant non-mammalian GnRH analogs and therapeutic uses thereof)

RN 60556-70-9 CAPLUS

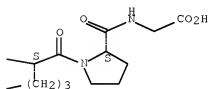
CN Luteinizing hormone-releasing factor (swine), 1-L-glutamic acid-10-glycine- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



NH

L80 ANSWER 4 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:902199 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 141:374704

TITLE: Composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders

INVENTOR(S): Chang, Yan; Sasak, Vodek

PATENT ASSIGNEE(S): Glycogenesys, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091634	A1	20041028	WO 2004-US10675	20040407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG

US 20040023925	A1	20040205	US 2003-408723	20030407 <--
AU 2004229399	A1	20041028	AU 2004-229399	20040407
CA 2521649	A1	20041028	CA 2004-2521649	20040407
US 20040223971	A1	20041111	US 2004-819901	20040407
EP 1617849	A1	20060125	EP 2004-759200	20040407
EP 1617849	B1	20080618		

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JP 2006522163	T	20060928	JP 2006-509773	20040407
US 20080089959	A1	20080417	US 2007-803150	20070511

PRIORITY APPLN. INFO.:

US 2003-408723	A	20030407
US 2003-461006P	P	20030407
US 2003-474562P	P	20030530
US 2001-299991P	P	20010621 <--
US 2002-176235	A2	20020620 <--
US 2004-819901	B1	20040407
WO 2004-US10675	W	20040407

AB The present invention is directed to methods and compns. for augmenting treatment of cancers and other proliferative disorders. In particular embodiments, the invention combines the administration of an agent that inhibits the anti-apoptotic activity of galectin-3 (e.g., a 'galectin-3 inhibitor') so as to potentiate the toxicity of a chemotherapeutic agent. In certain preferred embodiments, the conjoint therapies of the present invention can be used to improve the efficacy of those chemotherapeutic agents whose cytotoxicity is influenced by the status of an anti-apoptotic Bcl-2 protein for the treated cell. For instance, galectin-3 inhibitors can be administered in combination with a chemotherapeutic agent that interferes with DNA replication fidelity or cell-cycle progression of cells undergoing unwanted proliferation.

ICM A61K031-70

CC 1-6 (Pharmacology)

Section cross-reference(s): 2, 15

IT Carcinoma

Mammary gland, neoplasm

(adenocarcinoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)

IT Ovary, neoplasm

(carcinoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)

IT Intestine, neoplasm

(colon; composition and uses of galectin antagonists to augment treatment of

cancer or other proliferative disorders)

IT Intestine, neoplasm

(colorectal; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)

IT Angiogenesis inhibitors

Antitumor agents

Bladder, neoplasm

Brain, neoplasm

Chemotherapy

Chronic lymphocytic leukemia

Combination chemotherapy

Cytotoxic agents
 Digestive tract, neoplasm
 Drug delivery systems
 Drug resistance
 Drug targets
 Human
 Hyperplasia
 Kidney, neoplasm
 Leukemia
 Liver, neoplasm
 Lung, neoplasm
 Lymphoma
 Mammary gland, neoplasm
 Mastocytoma
 Melanoma
 Multiple myeloma
 Neoplasm
 Ovary, neoplasm
 Pancreas, neoplasm
 Papilloma
 Pharynx, neoplasm
 Prostate gland, neoplasm
 Psoriasis
 Radiotherapy
 Sarcoma
 Skin, neoplasm
 Stomach, neoplasm

(composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)

- IT Neuroglia, neoplasm
 (glioblastoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT Mesothelium, neoplasm
 (mesothelioma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT Microtubule
 (microtubule inhibiting drug; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT Nerve, neoplasm
 (neuroblastoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT Kidney, neoplasm
 (renal cell carcinoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT Pharynx, neoplasm
 (squamous cell carcinoma; composition and uses of galectin antagonists to augment treatment of cancer or other proliferative disorders)
- IT 50-02-2, Dexamethasone 50-07-7, Mitomycin 50-18-0, Cytosar 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 51-21-8, Fluorouracil 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 57-63-6, 17 α -Ethinylestradiol 58-05-9, Leucovorin 58-18-4, Methyltestosterone 58-22-0, Testosterone 59-05-2, Methotrexate 64-86-8, Colchicine 68-96-2, Hydroxyprogesterone 71-58-9, Medroxyprogesteroneacetate 76-43-7, Fluoxymesterone 83-43-2, Methylprednisolone 84-17-3, Dienestrol 124-94-7, Triamcinolone

125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 127-31-1,
 Fludrocortisone 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3,
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 29767-20-2, Teniposide 31430-18-9, Nocodazole 33069-62-4, Taxol
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 Buserelin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 63612-50-0,
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 71486-22-1, Vinorelbine 82855-09-2, Combretastatin 83150-76-9,
 Octreotide 85622-93-1, Temozolomide 89778-26-7, Toremifene
 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5,
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RL: PAC (Pharmacological activity); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(composition and uses of galectin antagonists to augment treatment of cancer

or other proliferative disorders)

IT 53714-56-0, Leuprolide 57982-77-1, Buserelin

65807-02-5, Zoladex

RL: PAC (Pharmacological activity); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(composition and uses of galectin antagonists to augment treatment of cancer

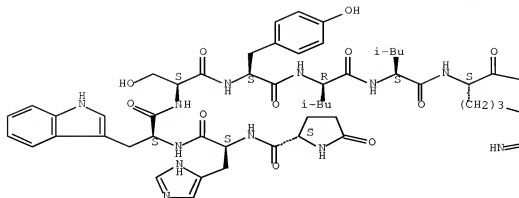
or other proliferative disorders)

RN 53714-56-0 CAPLUS

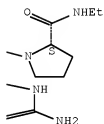
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

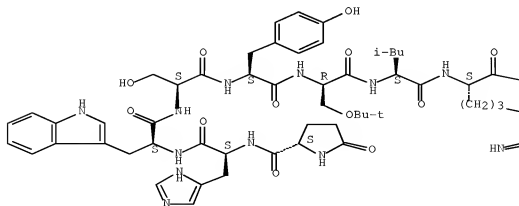


RN 57982-77-1 CAPLUS

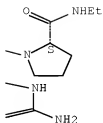
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

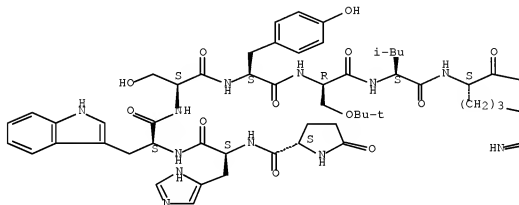


RN 65807-02-5 CAPLUS

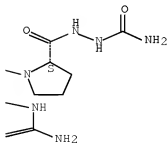
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 5 OF 52 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2004:100803 CAPLUS Full-text
 DOCUMENT NUMBER: 140:139483
 TITLE: Method for enhancing the effectiveness of therapies of hyperproliferative diseases
 INVENTOR(S): Chang, Yan; Sasak, Vodek
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 176,235.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040023925	A1	20040205	US 2003-408723	20030407 <--
US 20030013681	A1	20030116	US 2002-176235	20020620 <--
US 6680306	B2	20040120		
CN 1543351	A	20041103	CN 2002-816003	20020621 <--
US 20040043962	A1	20040304	US 2003-657383	20030908 <--
AU 2004229399	A1	20041028	AU 2004-229399	20040407
CA 2521649	A1	20041028	CA 2004-2521649	20040407
WO 2004091634	A1	20041028	WO 2004-US10675	20040407
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			US 2003-408723	A 20030407
			US 2003-461006P	P 20030407
			US 2003-474562P	P 20030530
			WO 2004-US10675	W 20040407
AB	The efficacy of conventional cancer therapies such as surgery, chemotherapy and radiation is enhanced by the use of a therapeutic material which binds to and interacts with galectins. The therapeutic material can enhance apoptosis thereby increasing the effectiveness of oncolytic agents. It can also inhibit angiogenesis thereby moderating tumor growth and/or metastasis.			
IC	ICM A61K031-732			
INCL	514054000			
CC	1-6 (Pharmacology)			
	Section cross-reference(s): 2, 7, 8, 15, 63			
ST	corticosteroid radiotherapeutic antibody modified pectin GCS100 antitumor			

resistance cancer
 IT Microtubule
 (- targeting drug; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Carcinoma
 Mammary gland, neoplasm
 (adenocarcinoma; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Drug resistance
 (antitumor; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Intestine, neoplasm
 (colon; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Intestine, neoplasm
 (colorectal; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Neuroglia, neoplasm
 (glioblastoma; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Neoplasm
 (metastasis; method for enhancing effectiveness of therapies of
 hyperproliferative diseases)
 IT Acute myeloid leukemia
 Angiogenesis
 Angiogenesis inhibitors
 Antitumor agents
 Apoptosis
 Bladder, neoplasm
 Brain, neoplasm
 Cell cycle
 Cell proliferation
 Chromatin
 Chronic lymphocytic leukemia
 DNA repair
 DNA replication
 Digestive tract, neoplasm
 Heat
 Human
 Intercalating agents
 Ionizing radiation
 Kidney, neoplasm
 Leukemia
 Leukemia
 Liver, neoplasm
 Lung, neoplasm
 Lymphoma
 Mammary gland, neoplasm
 Mastocytoma
 Melanoma
 Multiple myeloma
 Neoplasm
 Ovary, neoplasm
 Pancreas, neoplasm
 Papilloma
 Pharynx, neoplasm
 Prostate gland, neoplasm
 Sarcoma
 Signal transduction, biological
 Skin, neoplasm

Stomach, neoplasm

pH

(method for enhancing effectiveness of therapies of hyperproliferative diseases)

IT Nerve, neoplasm

(neuroblastoma; method for enhancing effectiveness of therapies of hyperproliferative diseases)

IT Kidney, neoplasm

(renal cell carcinoma; method for enhancing effectiveness of therapies of hyperproliferative diseases)

IT Antitumor agents

(resistance to; method for enhancing effectiveness of therapies of hyperproliferative diseases)

IT Pharynx, neoplasm

(squamous cell carcinoma; method for enhancing effectiveness of therapies of hyperproliferative diseases)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 51-21-8, 5-Fluorouracil 51-75-2 52-24-4, Triethylenethiophosphoramide 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristin 57-63-6, 17 α -Ethinylestradiol 58-05-9, Leucovorin 58-18-4, Methyl-testosterone 58-22-0, Testosterone 59-05-2, Methotrexate 64-86-8, Colchicine 68-96-2, Hydroxyprogesterone 71-58-9, Medroxyprogesteroneacetate 76-43-7, Fluoxymesterone 83-43-2, Methylprednisolone 84-17-3, Dienestrol 120-73-0D, Purine, analogs 124-94-7, Triamcinolone 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 127-31-1, Fludrocortisone 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 289-95-2D, Pyrimidine, analogs 302-79-4, Retinoin 305-03-3, Chlorambucil 446-72-0, Genistein 520-85-4, Medroxyprogesterone 521-12-0, Dromostanolone propionate 569-57-3, Chlorotrianisene 595-33-5, Megestrolacetate 645-05-6, Hexamethylmelamine 671-16-9, Procarbazine 865-21-4, Vinblastin 968-93-4, Testolactone 1271-19-8, Titanocene dichloride 1402-38-6, Actinomycin 1404-00-8, Mitomycin 1605-68-1, Taxane 2098-66-0, Cyproterone 2998-57-4, Estramustine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 7689-03-4, Camptothecin 8064-90-2, Cotrimoxazole 9015-68-3, Asparaginase 10540-29-1, Tamoxifen 10596-23-3 11056-06-7, Bleomycin 13010-20-3, Nitrosourea 13010-47-4, Lomustine 13311-84-7, Flutamide 14769-73-4, Levamisole 15663-27-1, Cisplatin 18378-89-7, Plicamycin 18883-66-4, Streptozocin 19767-45-4, Mesna 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 29767-20-2, Teniposide 31430-18-9, Nocodazole 33069-62-4, Paclitaxel 33419-42-0, Etoposide 40391-99-9 41575-94-4, Carboplatin 51264-14-3, Amsacrine 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin 57992-77-1, Buserelin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 63612-50-0, Nilutamide 65271-80-9, Mitoxantrone 65807-02-5, Goserelin 68335-15-9, Porfimer 71486-22-1, Vinorelbine 82855-09-2D, Combretastatin, compds. 83150-76-9, Octreotide 85622-93-1, Temozolomide 89778-26-7, Toremifene 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 107868-30-4, Exemestane 112809-51-5, Letrozole 112887-68-0, Raltitrexed 114977-28-5, Docetaxel 120511-73-1, Anastrozole 121181-53-1, Filgrastim 123948-87-8, Topotecan 125317-39-7, Navelbine 145781-92-6, Goserelin acetate 152459-95-5, Imatinib 154361-50-9, Capecitabine 174722-31-7, Rituximab 180288-69-1, Trastuzumab 183321-74-6 184475-35-2, ZD1839

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 531508-98-2, GCS-100 557795-19-4, SU11248 651768-96-6, OS 1774
 RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)
 (method for enhancing effectiveness of therapies of hyperproliferative
 diseases)

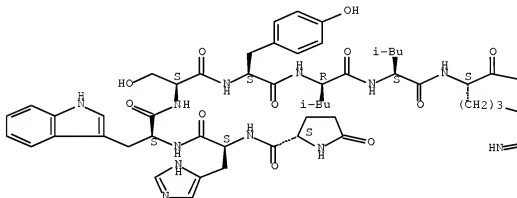
IT 53714-56-0, Leuprolide 57932-77-1, Buserelin
 65307-02-5, Goserelin 145731-92-6, Goserelin acetate
 RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)
 (method for enhancing effectiveness of therapies of hyperproliferative
 diseases)

RN 53714-56-0 CAPLUS

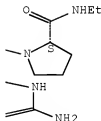
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-
 prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

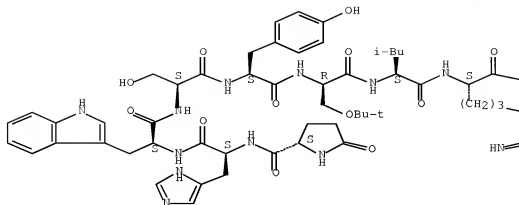


RN 57982-77-1 CAPLUS

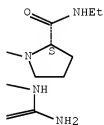
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-
 D-serine]-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

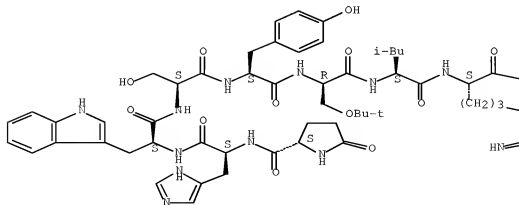


RN 65807-02-5 CAPLUS

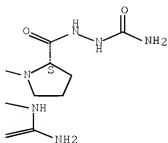
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B



RN 145781-92-6 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide, acetate (1:?) (CA INDEX NAME)

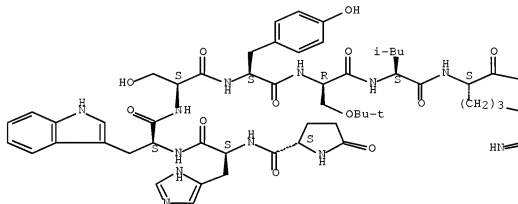
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CRN 65807-02-5

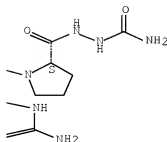
CMF C59 H84 N18 O14

Absolute stereochemistry.

PAGE 1-A



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CM 2

CRN 64-19-7

CMF C2 H4 O2



L80 ANSWER 6 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:3450 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:99617

TITLE: Peptide conjugates with drugs as prodrugs for activation by tissue or cell-specific proteinases
 INVENTOR(S): Madison, Edwin L.; Semple, Joseph Edward; Vlasuk, George P.; Kemp, Scott Jeffrey; Komandla, Mallareddy; Siev, Daniel Vanna

PATENT ASSIGNEE(S): Corvas International, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 359 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040001801	A1	20040101	US 2002-156214	20020523 <--
PRIORITY APPLN. INFO.:			US 2002-156214	20020523 <--

OTHER SOURCE(S): MARPAT 140:99617

AB Conjugates of peptides with drugs that are substrates of a tissue-specific proteinases that can be used to treat diseases associated with abnormal levels of the enzyme. The enzyme may be transmembrane serine proteinase, a urokinase, or an endotheliase. The conjugates are to be substrates for proteinases that may be cell- or tissue-specific. The drug moiety of the conjugate may be cytotoxic. The drug may be bound to the peptide by a labile linker that will eliminate itself after the preliminary hydrolysis.

IC ICM A61K038-20
 ICS A61K038-19; A61K038-18; C07K014-52; C07K014-475; C07K014-415; A61K039-02

INCL 424085100; 530351000; 530370000; 530395000; 530399000; 424085200;

514008000; 514012000; 424236100
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 3, 7
 IT Microtubule
 (antagonists, peptide conjugates, as prodrugs; peptide conjugates with
 drugs as prodrugs for activation by tissue or cell-specific
 proteinases)
 IT Intestine, neoplasm
 (colon, treatment of; peptide conjugates with drugs as prodrugs for
 activation by tissue or cell-specific proteinases)
 IT Prostate-specific antigen
 RL: MSC (Miscellaneous)
 (drug conjugates with peptides resistant to cleavage by;
 peptide conjugates with drugs as prodrugs for activation by tissue or
 cell-specific proteinases)
 IT Alkylating agents, biological
 Angiogenesis inhibitors
 Antitumor agents
 Cytotoxic agents
 (peptide conjugates, as prodrugs; peptide conjugates with drugs as
 prodrugs for activation by tissue or cell-specific proteinases)
 IT Autoimmune disease
 Endocrine system, disease
 Esophagus, neoplasm
 Eye, disease
 Glaucoma (disease)
 Heart, disease
 Infection
 Inflammation
 Lung, neoplasm
 Mammary gland, neoplasm
 Melanoma
 Neoplasm
 Ovary, neoplasm
 Pancreas, neoplasm
 Prostate gland, neoplasm
 Psoriasis
 Rheumatoid arthritis
 Skin, disease
 Wound
 (treatment of; peptide conjugates with drugs as prodrugs for activation
 by tissue or cell-specific proteinases)
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IT 9001-90-5, Plasmin
 RL: MSC (Miscellaneous)
 (drug conjugates with peptides resistant to cleavage by;
 peptide conjugates with drugs as prodrugs for activation by tissue or
 cell-specific proteinases)

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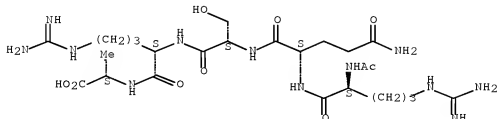
RL: BSU (Biological study, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence, as prodrug; peptide conjugates with drugs as
 prodrugs for activation by tissue or cell-specific proteinases)

RN 476678-22-5 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

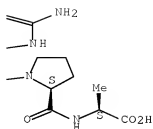


RN 476678-22-5 CAPLUS

CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-
 arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

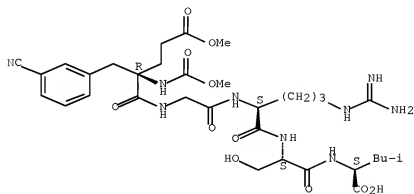
PAGE 1-B



RN 476681-34-2 CAPLUS

CN L-Leucine, 2-[(3-cyanophenyl)methyl]-N-(methoxycarbonyl)-L- α -glutamylglycyl-L-arginyl-L-seryl-, 1-methyl ester (9CI) (CA INDEX NAME)

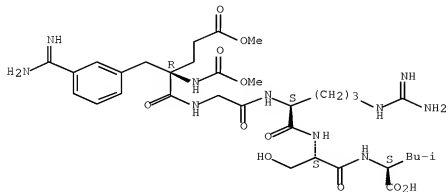
Absolute stereochemistry.



RN 476681-35-3 CAPLUS

CN L-Leucine, 2-[[3-(aminoiminomethyl)phenyl]methyl]-N-(methoxycarbonyl)-L- α -glutamylglycyl-L-arginyl-L-seryl-, 1-methyl ester (9CI) (CA INDEX NAME)

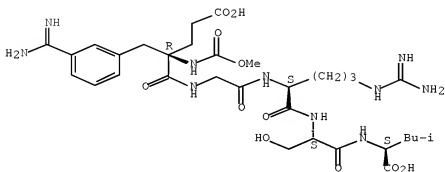
Absolute stereochemistry.



RN 476681-36-4 CAPLUS

CN L-Leucine, 2-[[3-(aminoiminomethyl)phenyl]methyl]-N-(methoxycarbonyl)-L- α -glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

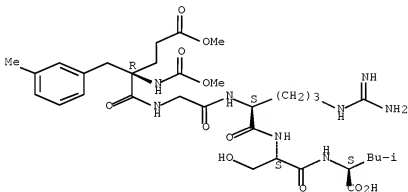
Absolute stereochemistry.



RN 476681-37-5 CAPLUS

CN L-Leucine, N-(methoxycarbonyl)-2-[(3-methylphenyl)methyl]-L- α -glutamylglycyl-L-arginyl-L-seryl-, 1-methyl ester (9CI) (CA INDEX NAME)

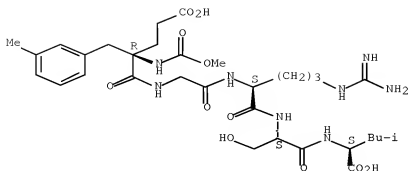
Absolute stereochemistry.



RN 476681-38-6 CAPLUS

CN L-Leucine, N-(methoxycarbonyl)-2-[(3-methylphenyl)methyl]-L- α -glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

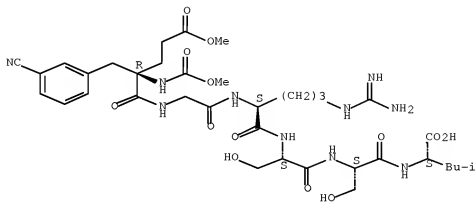
Absolute stereochemistry.



RN 476681-39-7 CAPLUS

CN L-Leucine, 2-[(3-cyanophenyl)methyl]-N-(methoxycarbonyl)-L-α-glutamylglycyl-L-arginyl-L-seryl-L-seryl-, 1-methyl ester (9CI) (CA INDEX NAME)

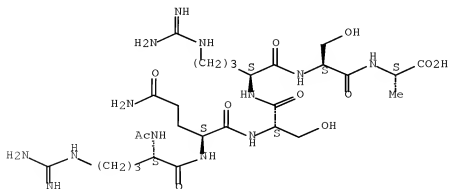
Absolute stereochemistry.



RN 476681-99-9 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl-L-seryl-, (9CI) (CA INDEX NAME)

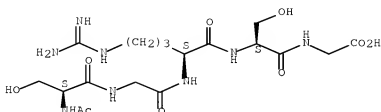
Absolute stereochemistry.



RN 476682-05-0 CAPLUS

CN Glycine, N-acetyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

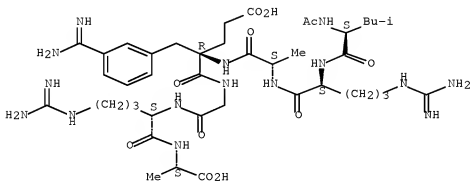
Absolute stereochemistry.



RN 642482-56-2 CAPLUS

CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl)methyl]-L- α -glutamylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

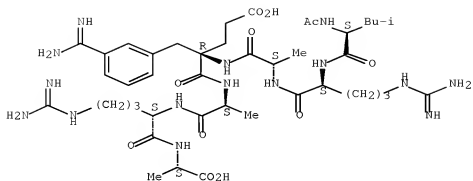
Absolute stereochemistry.



RN 642482-58-4 CAPLUS

CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl)methyl]-L- α -glutamyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

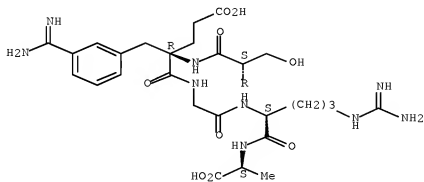


RN 642482-60-8 CAPLUS

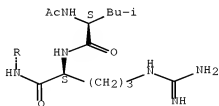
CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[(3-(aminoiminomethyl)phenyl)methyl]-L-α-glutamylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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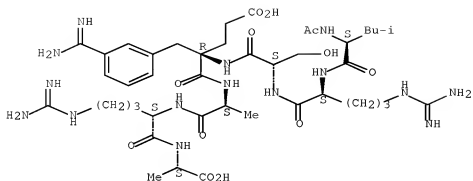
PAGE 2-A



RN 642482-61-9 CAPLUS

CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[(3-(aminoiminomethyl)phenyl)methyl]-L-α-glutamyl-L-alanyl-L-arginyl- (9CI)
(CA INDEX NAME)

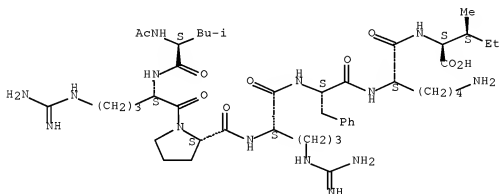
Absolute stereochemistry.



RN 642482-62-0 CAPLUS

CN L-Isoleucine, N-acetyl-L-leucyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

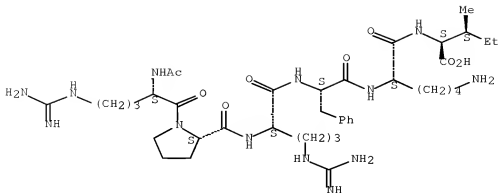
Absolute stereochemistry.



RN 642482-64-2 CAPLUS

CN L-Isoleucine, N2-acetyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

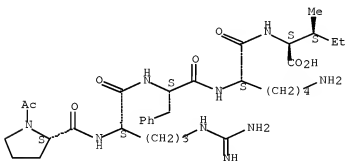
Absolute stereochemistry.



RN 642482-65-3 CAPLUS

CN L-Isoleucine, 1-acetyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

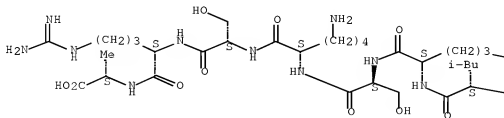


RN 642482-66-4 CAPLUS

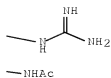
CN L-Alanine, N-acetyl-L-leucyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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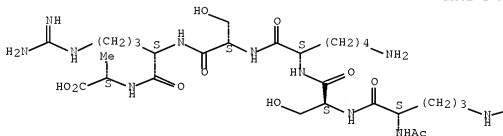


RN 642482-67-5 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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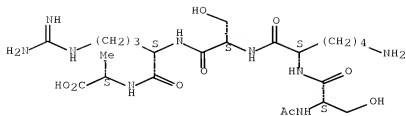
PAGE 1-B



RN 642482-68-6 CAPLUS

CN L-Alanine, N-acetyl-L-seryl-L-lysyl-L-seryl-L-arginyl- (9CI) (CA INDEX
NAME)

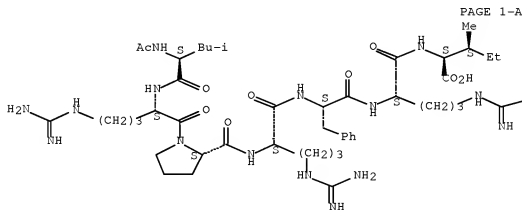
Absolute stereochemistry.



RN 642482-69-7 CAPLUS

CN L-Isoleucine, N-acetyl-L-leucyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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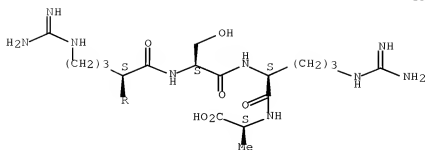
NH2

RN 642482-70-0 CAPLUS

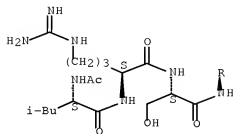
CN L-Isoleucine, N2-acetyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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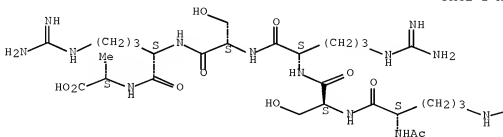


RN 642482-73-3 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-seryl-L-arginyl-L-seryl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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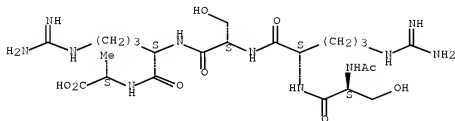




RN 642482-74-4 CAPLUS

CN L-Alanine, N-acetyl-L-seryl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

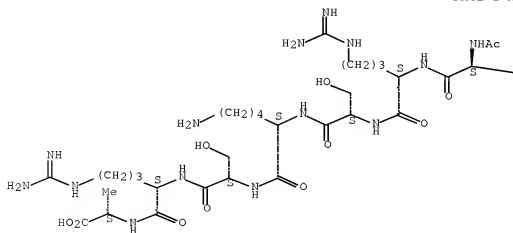
Absolute stereochemistry.

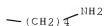


RN 642482-75-5 CAPLUS

CN L-Alanine, N2-acetyl-L-lysyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

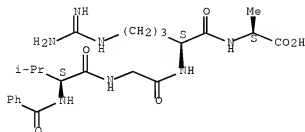




RN 642482-78-8 CAPLUS

CN L-Alanine, N-benzoyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

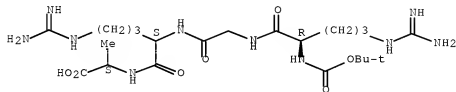
Absolute stereochemistry.



RN 642482-79-9 CAPLUS

CN L-Alanine, N2-[(1,1-dimethylethoxy)carbonyl]-D-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

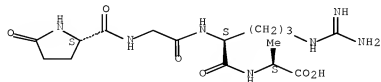
Absolute stereochemistry.



RN 642482-80-2 CAPLUS

CN L-Alanine, 5-oxo-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

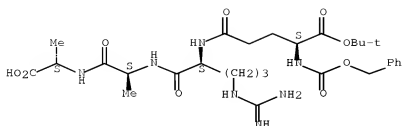
Absolute stereochemistry.



RN 642482-82-4 CAPLUS

CN L-Alanine, N-[(phenylmethoxy)carbonyl]-L-γ-glutamyl-L-arginyl-L-alanyl-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

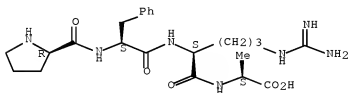
Absolute stereochemistry.



RN 642482-83-5 CAPLUS

CN L-Alanine, D-prolyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

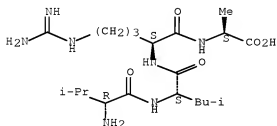
Absolute stereochemistry.



RN 642482-84-6 CAPLUS

CN L-Alanine, D-valyl-L-leucyl-L-arginyl- (9CI) (CA INDEX NAME)

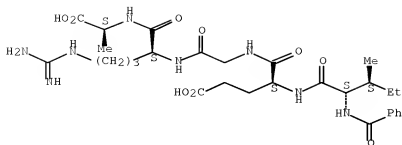
Absolute stereochemistry.



RN 642482-85-7 CAPLUS

CN L-Alanine, N-benzoyl-L-isoleucyl-L- α -glutamylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

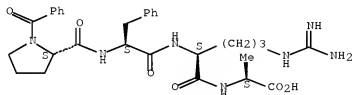
Absolute stereochemistry.



RN 642482-86-8 CAPLUS

CN L-Alanine, 1-benzoyl-L-prolyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

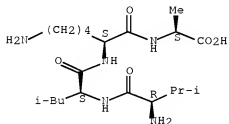
Absolute stereochemistry.



RN 642482-88-0 CAPLUS

CN L-Alanine, D-valyl-L-leucyl-L-lysyl- (9CI) (CA INDEX NAME)

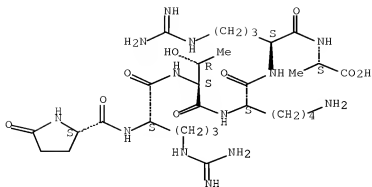
Absolute stereochemistry.



RN 642482-89-1 CAPLUS

CN L-Alanine, 5-oxo-L-prolyl-L-arginyl-L-threonyl-L-lysyl-L-arginyl- (9CI) (CA INDEX NAME)

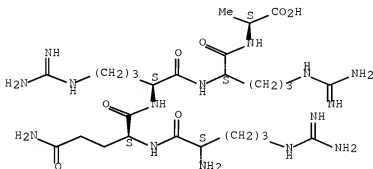
Absolute stereochemistry.



RN 642482-90-4 CAPLUS

CN L-Alanine, L-arginyl-L-glutamyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

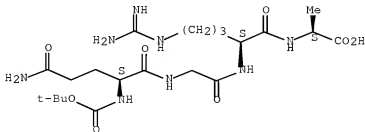
Absolute stereochemistry.



RN 642482-91-5 CAPLUS

CN L-Alanine, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutamylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

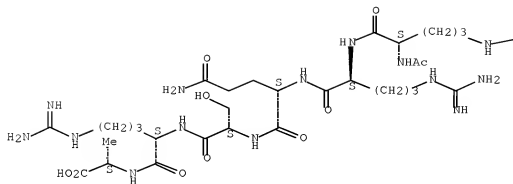


RN 642482-95-9 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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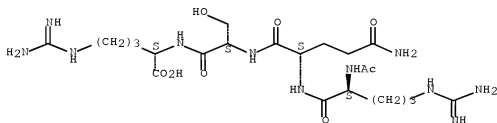


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RN 642482-96-0 CAPLUS
 CN L-Arginine, N2-acetyl-L-arginyl-L-glutamyl-L-seryl- (9CI) (CA INDEX NAME)

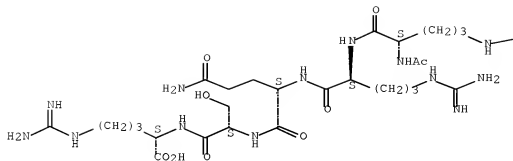
Absolute stereochemistry.



RN 642482-97-1 CAPLUS
 CN L-Arginine, N2-acetyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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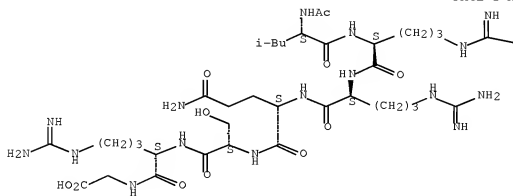


RN 642482-98-2 CAPLUS

CN Glycine, N-acetyl-L-leucyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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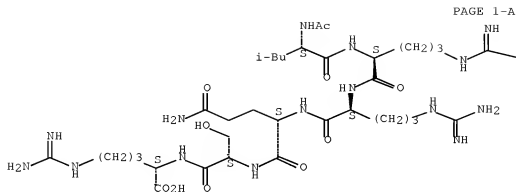


RN 642482-99-3 CAPLUS

CN L-Arginine, N-acetyl-L-leucyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



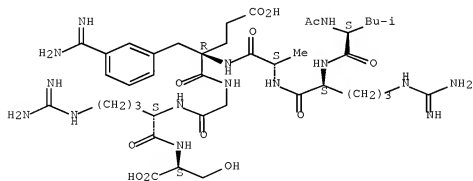
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NH₂

RN 642483-00-9 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

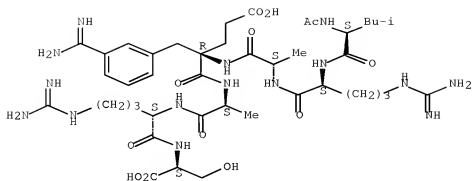
Absolute stereochemistry.



RN 642483-01-0 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

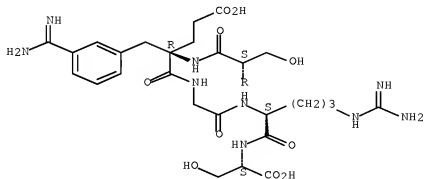


RN 642483-02-1 CAPLUS

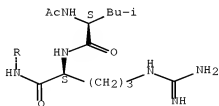
CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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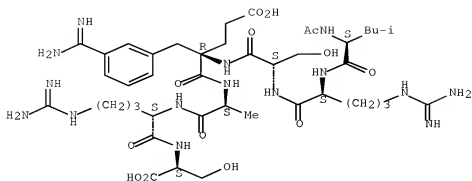
PAGE 2-A



RN 642483-03-2 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

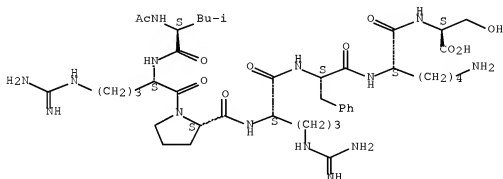
Absolute stereochemistry.



RN 642483-04-3 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

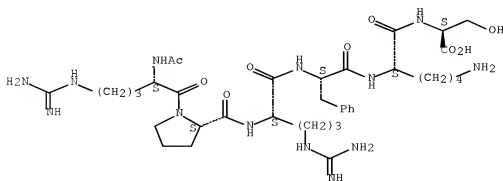
Absolute stereochemistry.



RN 642483-05-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

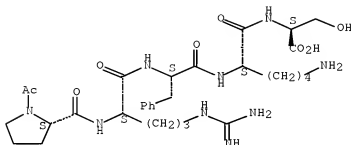
Absolute stereochemistry.



RN 642483-06-5 CAPLUS

CN L-Serine, 1-acetyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

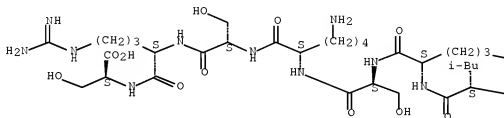


RN 642483-07-6 CAPLUS

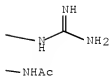
CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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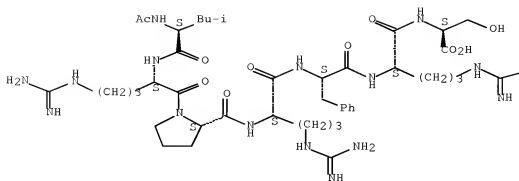


RN 642483-08-7 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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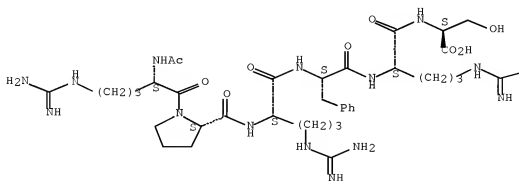
—NH₂

RN 642483-11-2 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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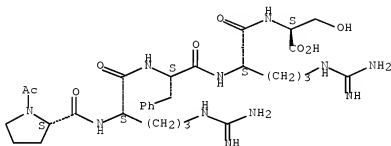




RN 642483-12-3 CAPLUS

CN L-Serine, 1-acetyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

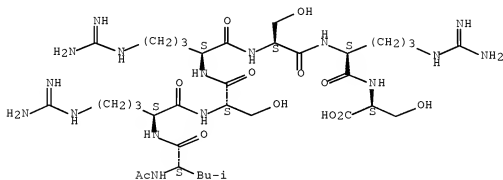
Absolute stereochemistry.



RN 642483-13-4 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

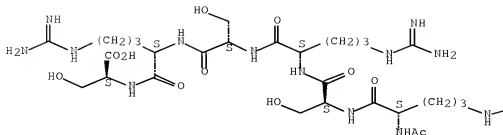


RN 642483-14-5 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-seryl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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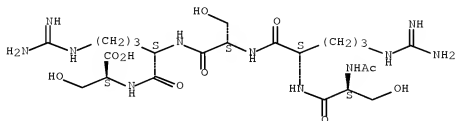
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RN 642483-16-7 CAPLUS

CN L-Serine, N-acetyl-L-seryl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

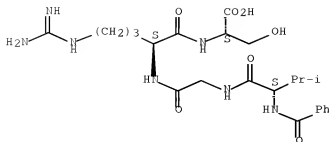
Absolute stereochemistry.



RN 642483-22-5 CAPLUS

CN L-Serine, N-benzoyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

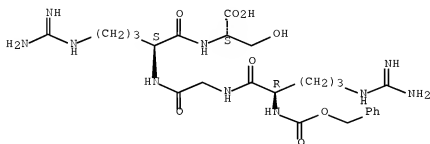
Absolute stereochemistry.



RN 642483-23-6 CAPLUS

CN L-Serine, N2-[(phenylmethoxy)carbonyl]-D-arginylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

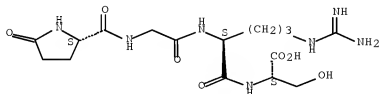
Absolute stereochemistry.



RN 642483-24-7 CAPLUS

CN L-Serine, 5-oxo-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

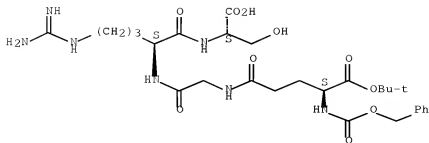
Absolute stereochemistry.



RN 642483-26-9 CAPLUS

CN L-Serine, N-[(phenylmethoxy)carbonyl]-L-gutamylglycyl-L-arginyl-,
1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

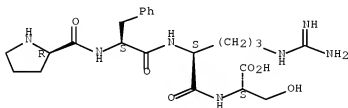
Absolute stereochemistry.



RN 642483-27-0 CAPLUS

CN L-Serine, D-prolyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

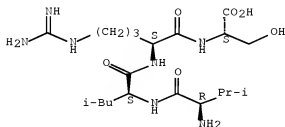
Absolute stereochemistry.



RN 642483-28-1 CAPLUS

CN L-Serine, D-valyl-L-leucyl-L-arginyl- (9CI) (CA INDEX NAME)

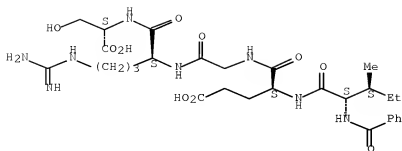
Absolute stereochemistry.



RN 642483-29-2 CAPLUS

CN L-Serine, N-benzoyl-L-isoleucyl-L-α-glutamylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

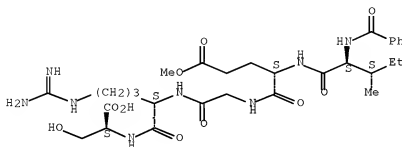
Absolute stereochemistry.



RN 642483-30-5 CAPLUS

CN L-Serine, N-benzoyl-L-isoleucyl-L-α-glutamylglycyl-L-arginyl-,
2-methyl ester (9CI) (CA INDEX NAME)

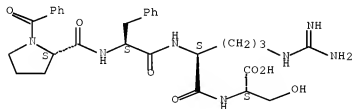
Absolute stereochemistry.



RN 642483-31-6 CAPLUS

CN L-Serine, 1-benzoyl-L-prolyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX
NAME)

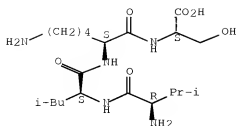
Absolute stereochemistry.



RN 642483-33-8 CAPLUS

CN L-Serine, D-valyl-L-leucyl-L-lysyl- (9CI) (CA INDEX NAME)

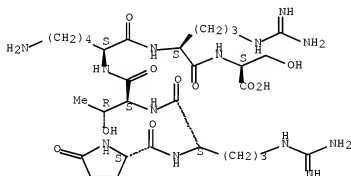
Absolute stereochemistry.



RN 642483-34-9 CAPLUS

CN L-Serine, 5-oxo-L-prolyl-L-arginyl-L-threonyl-L-lysyl-L-arginyl- (9CI)
(CA INDEX NAME)

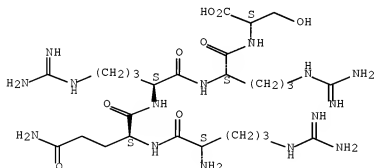
Absolute stereochemistry.



RN 642483-35-0 CAPLUS

CN L-Serine, L-arginyl-L-glutamyl-L-arginyl-L-arginyl- (9CI) (CA INDEX
NAME)

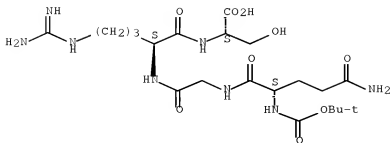
Absolute stereochemistry.



RN 642483-36-1 CAPLUS

CN L-Serine, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutamylglycyl-L-arginyl-
(9CI) (CA INDEX NAME)

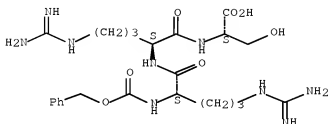
Absolute stereochemistry.



RN 642483-37-2 CAPLUS

CN L-Serine, N2-[(phenylmethoxy)carbonyl]-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

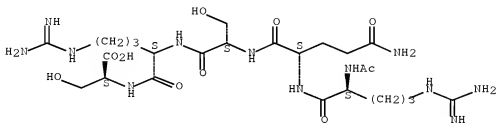
Absolute stereochemistry.



RN 642483-40-7 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

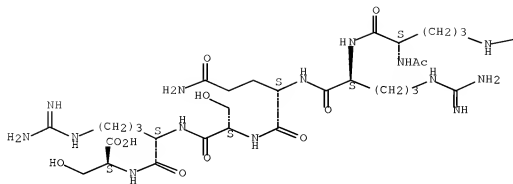


RN 642483-41-8 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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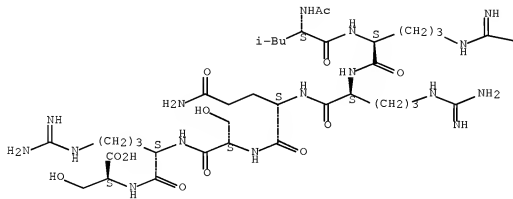


RN 642483-42-9 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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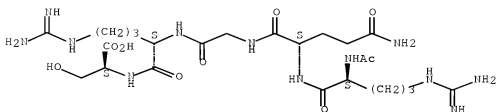
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RN 642483-43-0 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyglycyl-L-arginyl- (9CI) (CA INDEX NAME)

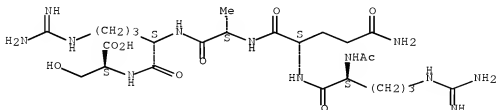
Absolute stereochemistry.



RN 642483-44-1 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminy-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

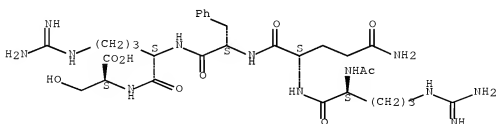
Absolute stereochemistry.



RN 642483-45-2 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminy-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

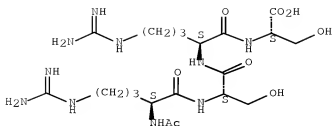
Absolute stereochemistry.



RN 642483-46-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

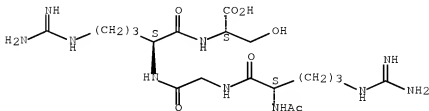
Absolute stereochemistry.



RN 642483-47-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

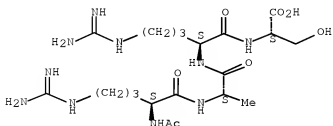
Absolute stereochemistry.



RN 642483-48-5 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

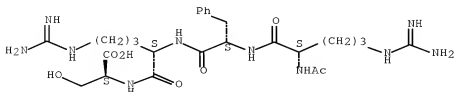
Absolute stereochemistry.



RN 642483-49-6 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

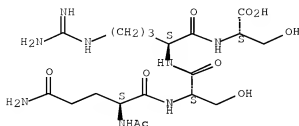
Absolute stereochemistry.



RN 642483-50-9 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminy-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

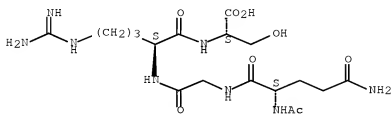
Absolute stereochemistry.



RN 642483-51-0 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminyglycyl-L-arginyl- (9CI) (CA INDEX NAME)

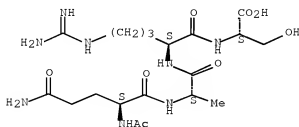
Absolute stereochemistry.



RN 642483-52-1 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminy-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

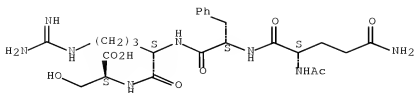
Absolute stereochemistry.



RN 642483-53-2 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminy-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

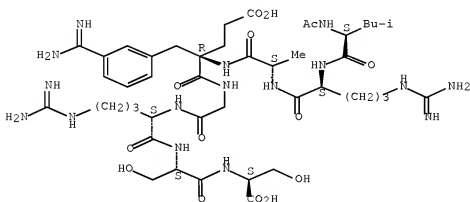
Absolute stereochemistry.



RN 642483-54-3 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

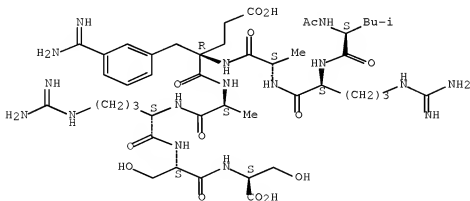
Absolute stereochemistry.



RN 642483-55-4 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-alanyl-2-[[3-(aminoiminomethyl)phenyl]methyl]-L-α-glutamyl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

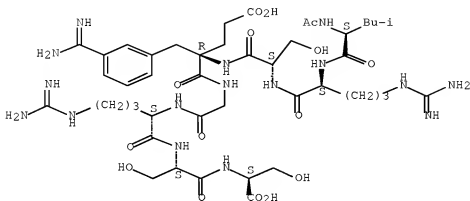


RN 642483-56-5 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[[3-

(aminoiminomethyl)phenyl)methyl]-L- α -glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

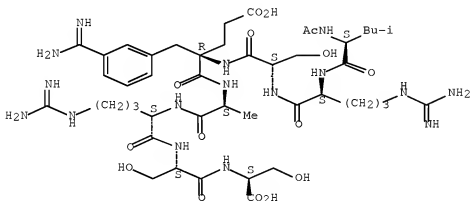
Absolute stereochemistry.



RN 642483-57-6 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-2-[[3-(aminoiminomethyl)phenyl)methyl]-L- α -glutamyl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 642483-58-7 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

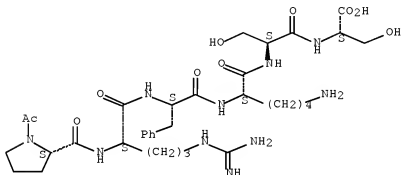
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RN 642483-60-1 CAPLUS

CN L-Serine, 1-acetyl-L-prolyl-L-arginyl-L-phenylalanyl-L-lysyl-L-seryl-
(9CI) (CA INDEX NAME)

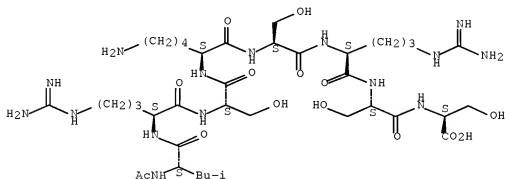
Absolute stereochemistry.



RN 642483-61-2 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl-L-
seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

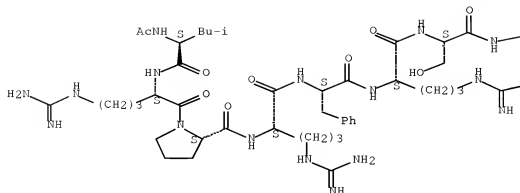


RN 642483-62-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-seryl-L-lysyl-L-seryl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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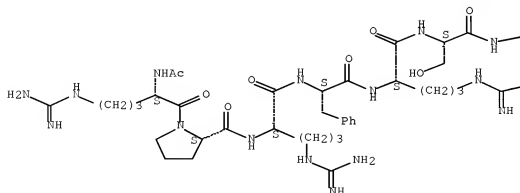


RN 642483-65-6 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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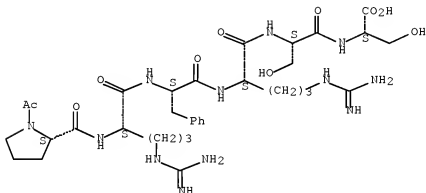
PAGE 1-B



RN 642483-66-7 CAPLUS

CN L-Serine, 1-acetyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

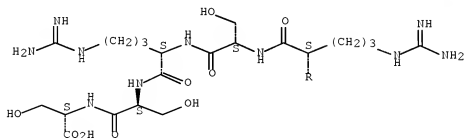


RN 642483-67-8 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-seryl-L-arginyl-L-seryl-L-arginyl-
L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

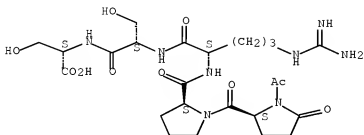
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RN 642483-72-5 CAPLUS

CN L-Serine, 1-acetyl-5-oxo-L-prolyl-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

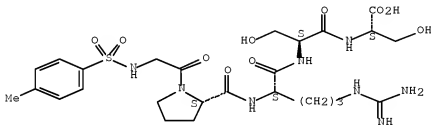
Absolute stereochemistry.



RN 642483-73-6 CAPLUS

CN L-Serine, N-[(4-methylphenyl)sulfonyl]glycyl-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

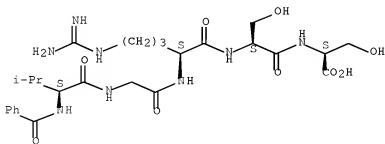
Absolute stereochemistry.



RN 642483-74-7 CAPLUS

CN L-Serine, N-benzoyl-L-valylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

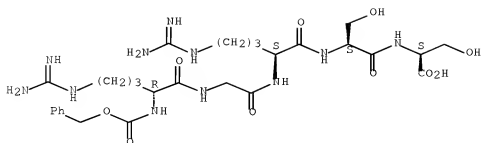
Absolute stereochemistry.



RN 642483-75-8 CAPLUS

CN L-Serine, N2-[(phenylmethoxy)carbonyl]-D-arginylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

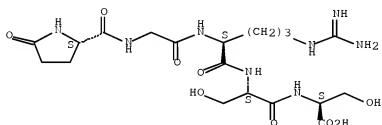
Absolute stereochemistry.



RN 642483-76-9 CAPLUS

CN L-Serine, 5-oxo-L-prolylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

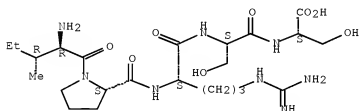
Absolute stereochemistry.



RN 642483-77-0 CAPLUS

CN L-Serine, D-isoleucyl-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

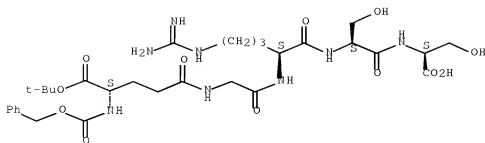
Absolute stereochemistry.



RN 642483-78-1 CAPLUS

CN L-Serine, N-[(phenylmethoxy)carbonyl]-L-gutamylglycyl-L-arginyl-L-seryl-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

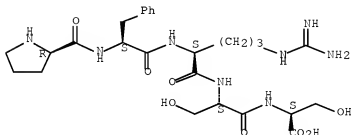
Absolute stereochemistry.



RN 642483-79-2 CAPLUS

CN L-Serine, D-prolyl-L-phenylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

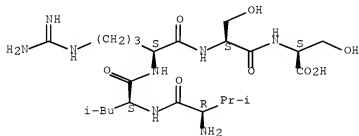
Absolute stereochemistry.



RN 642483-80-5 CAPLUS

CN L-Serine, D-valyl-L-leucyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

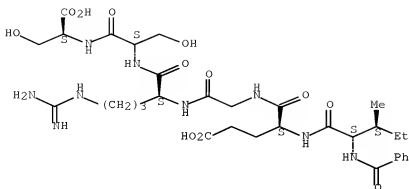
Absolute stereochemistry.



RN 642483-81-6 CAPLUS

CN L-Serine, N-benzoyl-L-isoleucyl-L- α -glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

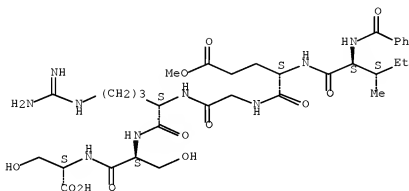
Absolute stereochemistry.



RN 642483-82-7 CAPLUS

CN L-Serine, N-benzoyl-L-isoleucyl-L-α-glutamylglycyl-L-arginyl-L-seryl-, 2-methyl ester (9CI) (CA INDEX NAME)

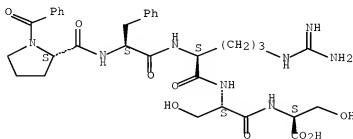
Absolute stereochemistry.



RN 642483-83-8 CAPLUS

CN L-Serine, 1-benzoyl-L-prolyl-L-phenylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

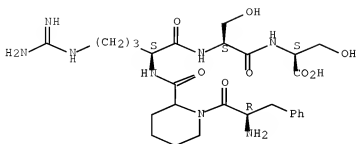
Absolute stereochemistry.



RN 642483-84-9 CAPLUS

CN L-Serine, D-phenylalanyl-2-piperidinecarbonyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

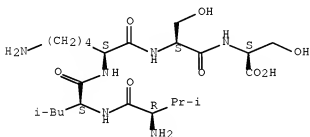
Absolute stereochemistry.



RN 642483-85-0 CAPLUS

CN L-Serine, D-valyl-L-leucyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

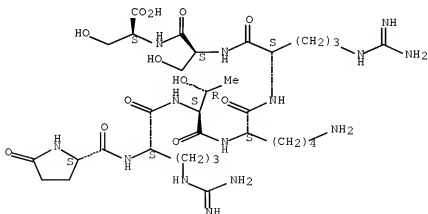
Absolute stereochemistry.



RN 642483-86-1 CAPLUS

CN L-Serine, 5-oxo-L-prolyl-L-arginyl-L-threonyl-L-lysyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

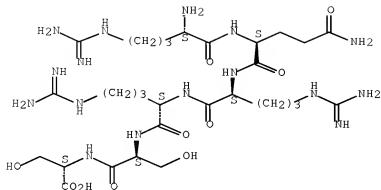
Absolute stereochemistry.



RN 642483-87-2 CAPLUS

CN L-Serine, L-arginyl-L-glutamyl-L-arginyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

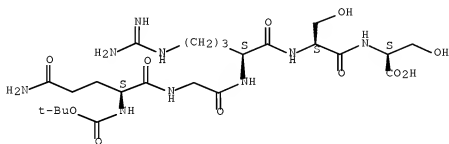
Absolute stereochemistry.



RN 642483-88-3 CAPLUS

CN L-Serine, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutaminyglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

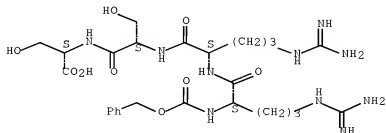
Absolute stereochemistry.



RN 642483-89-4 CAPLUS

CN L-Serine, N2-[(phenylmethoxy)carbonyl]-L-arginyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

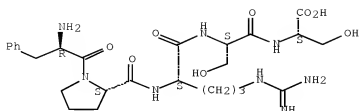
Absolute stereochemistry.



RN 642483-90-7 CAPLUS

CN L-Serine, D-phenylalanyl-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

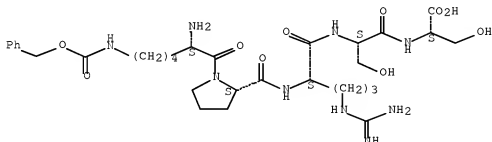
Absolute stereochemistry.



RN 642483-91-8 CAPLUS

CN L-Serine, N6-[1(phenylmethoxy)carbonyl]-L-lysyl-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

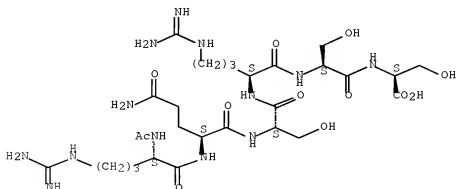
Absolute stereochemistry.



RN 642483-92-9 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyl-L-seryl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

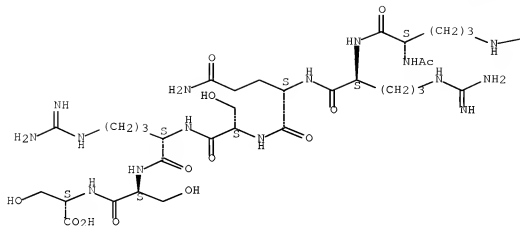


RN 642483-93-0 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-arginyl-L-glutaminyl-L-seryl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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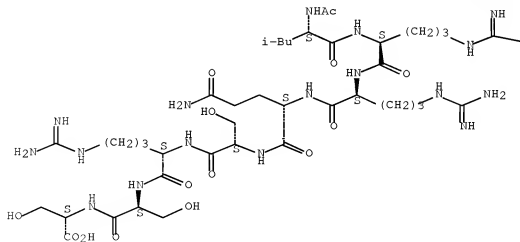


RN 642483-94-1 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginyl-L-arginyl-L-glutamyl-L-seryl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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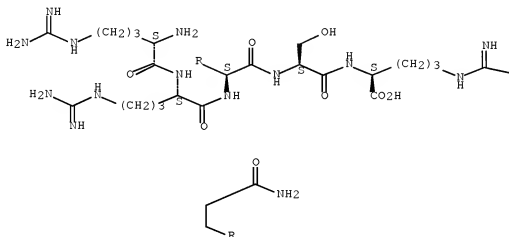
—NH₂

RN 642483-95-2 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-L-glutaminyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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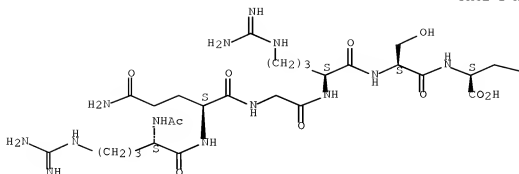
—NH₂

RN 642483-96-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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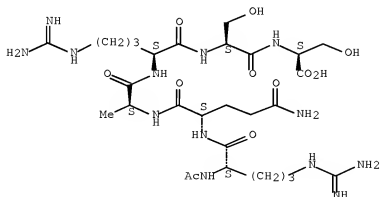
PAGE 1-B

—OH

RN 642483-97-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyl-L-alanyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

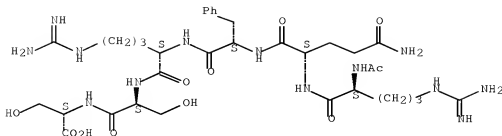
Absolute stereochemistry.



RN 642483-98-5 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyl-L-phenylalanyl-L-arginyl-L-
seryl- (9CI) (CA INDEX NAME)

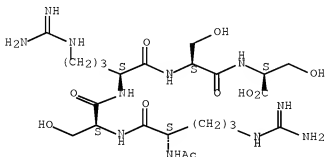
Absolute stereochemistry.



RN 642483-99-6 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-seryl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

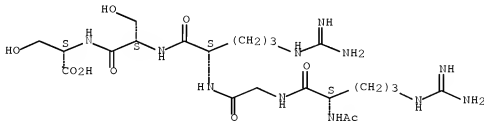
Absolute stereochemistry.



RN 642484-00-2 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

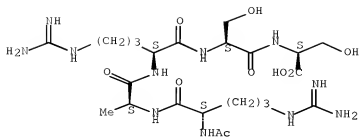
Absolute stereochemistry.



RN 642484-01-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

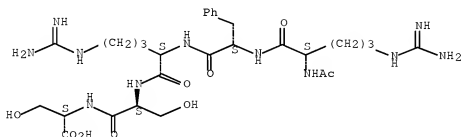
Absolute stereochemistry.



RN 642484-02-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-phenylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

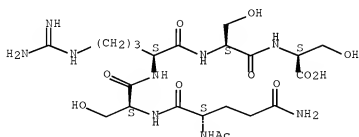
Absolute stereochemistry.



RN 642484-03-5 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-L-seryl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

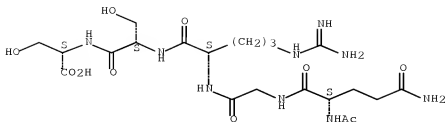
Absolute stereochemistry.



RN 642484-04-6 CAPLUS

CN L-Serine, N2-acetyl-L-glutamylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

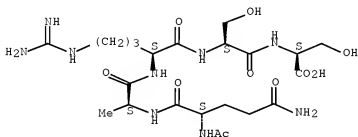
Absolute stereochemistry.



RN 642484-05-7 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

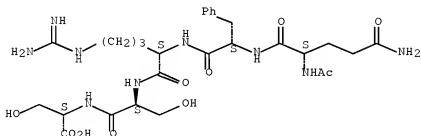
Absolute stereochemistry.



RN 642484-06-8 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-L-phenylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

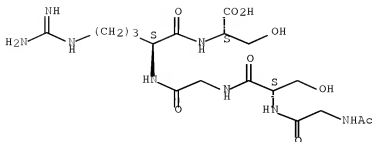
Absolute stereochemistry.



RN 642484-07-9 CAPLUS

CN L-Serine, N-acetylglycyl-L-serylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

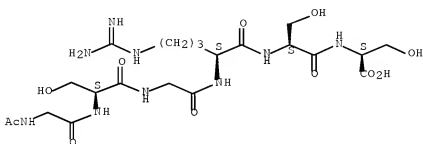
Absolute stereochemistry.



RN 642484-08-0 CAPLUS

CN L-Serine, N-acetylglycyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

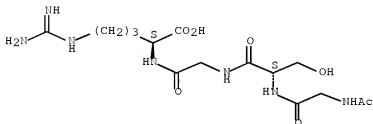
Absolute stereochemistry.



RN 642484-09-1 CAPLUS

CN L-Arginine, N-acetylglycyl-L-serylglycyl- (9CI) (CA INDEX NAME)

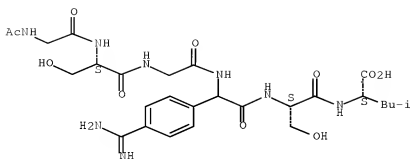
Absolute stereochemistry.



RN 642484-10-4 CAPLUS

CN L-Leucine, N-acetylglycyl-L-serylglycyl-2-[4-(aminoiminomethyl)phenyl]glycyl-L-seryl- (9CI) (CA INDEX NAME)

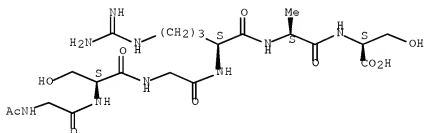
Absolute stereochemistry.



RN 642484-11-5 CAPLUS

CN L-Serine, N-acetylglucyl-L-serylglycyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

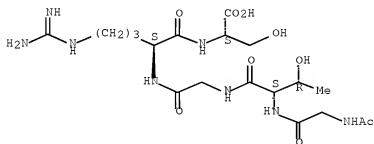
Absolute stereochemistry.



RN 642484-12-6 CAPLUS

CN L-Serine, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

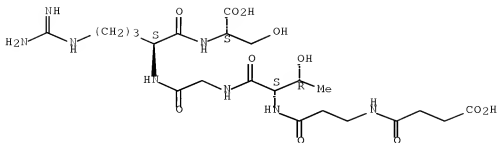
Absolute stereochemistry.



RN 642484-13-7 CAPLUS

CN L-Serine, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

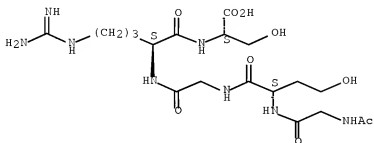
Absolute stereochemistry.



RN 642484-14-8 CAPLUS

CN L-Serine, N-acetylglycyl-L-homoserylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

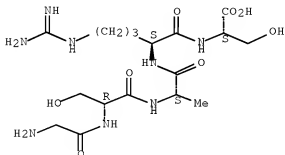
Absolute stereochemistry.



RN 642484-15-9 CAPLUS

CN L-Serine, glycy-L-D-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

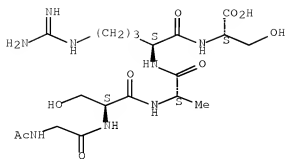
Absolute stereochemistry.



RN 642484-16-0 CAPLUS

CN L-Serine, N-acetylglycyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

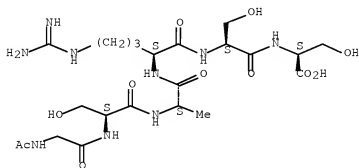
Absolute stereochemistry.



RN 642484-17-1 CAPLUS

CN L-Serine, N-acetylglycyl-L-seryl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

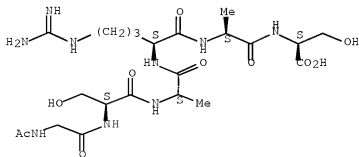
Absolute stereochemistry.



RN 642484-18-2 CAPLUS

CN L-Serine, N-acetylglycyl-L-seryl-L-alanyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

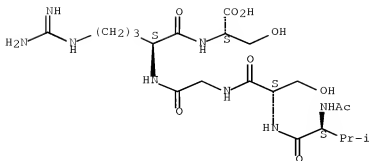
Absolute stereochemistry.



RN 642484-19-3 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

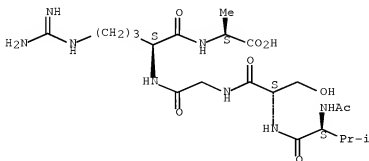
Absolute stereochemistry.



RN 642484-20-6 CAPLUS

CN L-Alanine, N-acetyl-L-valyl-L-serylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

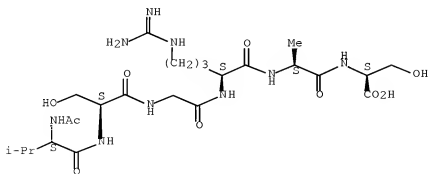
Absolute stereochemistry.



RN 642484-21-7 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-serylglycyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

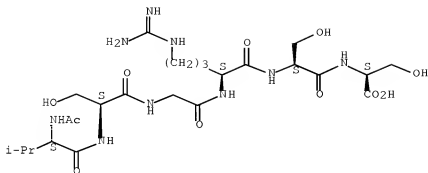
Absolute stereochemistry.



RN 642484-22-8 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

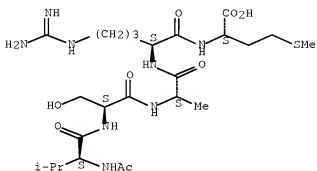
Absolute stereochemistry.



RN 642484-23-9 CAPLUS

CN L-Methionine, N-acetyl-L-valyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

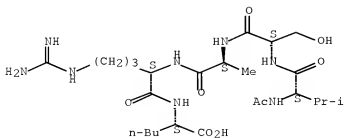
Absolute stereochemistry.



RN 642484-24-0 CAPLUS

CN L-Norleucine, N-acetyl-L-valyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

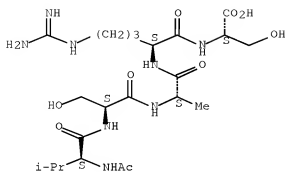
Absolute stereochemistry.



RN 642484-25-1 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

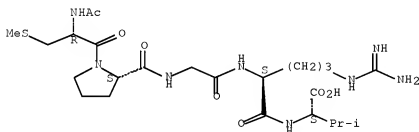
Absolute stereochemistry.



RN 642484-26-2 CAPLUS

CN L-Valine, N-acetyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

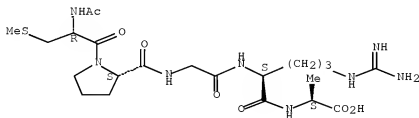
Absolute stereochemistry.



RN 642484-27-3 CAPLUS

CN L-Alanine, N-acetyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

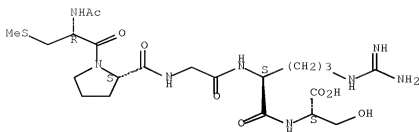
Absolute stereochemistry.



RN 642484-28-4 CAPLUS

CN L-Serine, N-acetyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

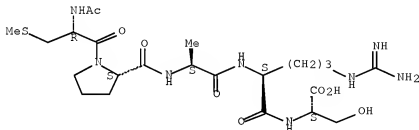
Absolute stereochemistry.



RN 642484-29-5 CAPLUS

CN L-Serine, N-acetyl-S-methyl-L-cysteinyl-L-prolyl-L-alanyl-L-arginyl- (9CI)
(CA INDEX NAME)

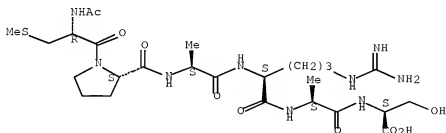
Absolute stereochemistry.



RN 642484-30-8 CAPLUS

CN L-Serine, N-acetyl-3-methyl-L-cysteinyl-L-prolyl-L-alanyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

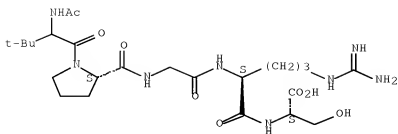
Absolute stereochemistry.



RN 642484-31-9 CAPLUS

CN L-Serine, N-acetyl-3-methyl-L-cysteinyl-L-prolyl-L-alanyl-L-arginyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

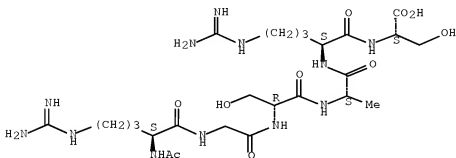
Absolute stereochemistry.



RN 642484-32-0 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-D-seryl-L-alanyl-L-argininyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

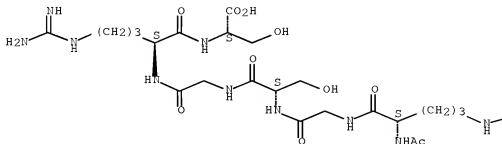


RN 642484-33-1 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-serylglycyl-L-argininyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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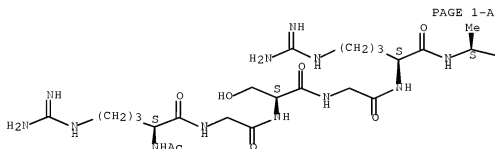
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RN 642484-34-2 CAPLUS

CN L-Alanine, N2-acetyl-L-arginylglycyl-L-serylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



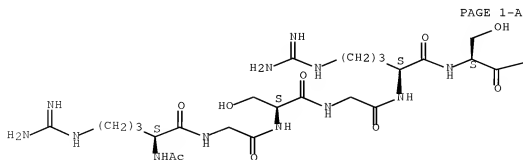
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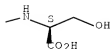
RN 642484-35-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



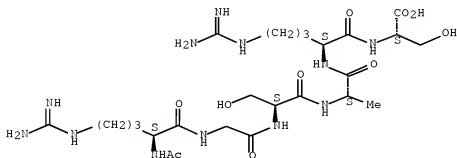
PAGE 1-B



RN 642484-36-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

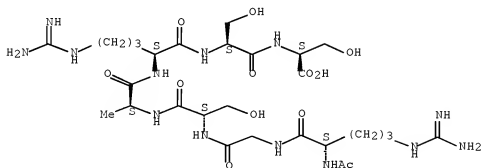
Absolute stereochemistry.



RN 642484-37-5 CAPLUS

CN L-Serine, N2-acetyl-L-arginylglycyl-L-seryl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

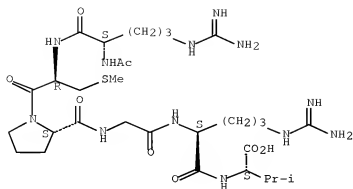
Absolute stereochemistry.



RN 642484-38-6 CAPLUS

CN L-Valine, N2-acetyl-L-arginyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

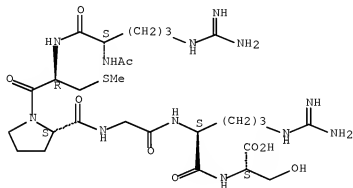
Absolute stereochemistry.



RN 642484-39-7 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

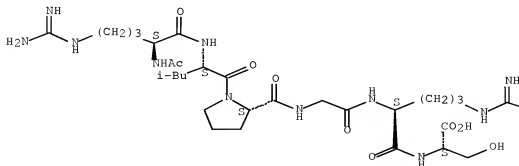


RN 642484-40-0 CAPLUS

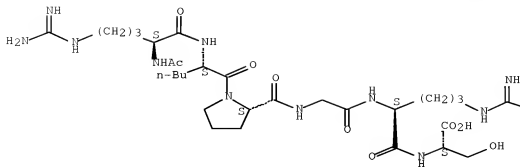
CN L-Serine, N2-acetyl-L-arginyl-L-leucyl-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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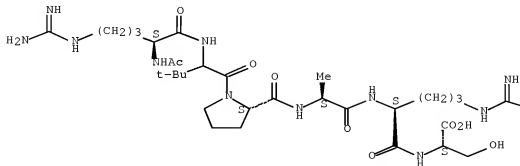
NH₂

RN 642484-43-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-3-methylvalyl-L-prolyl-L-alanyl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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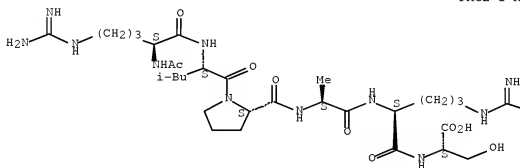
—NH₂

RN 642484-44-4 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-leucyl-L-prolyl-L-alanyl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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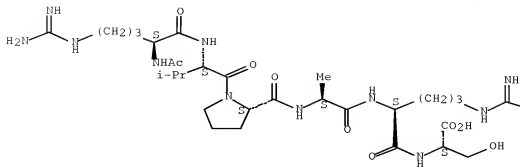
—NH₂

RN 642484-45-5 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-valyl-L-prolyl-L-alanyl-L-arginyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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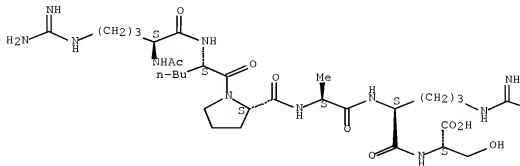
NH2

RN 642484-46-6 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-norleucyl-L-prolyl-L-alanyl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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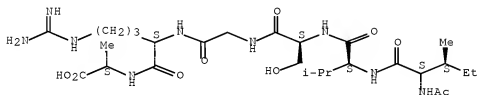
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RN 642484-47-7 CAPLUS

CN L-Alanine, N-acetyl-L-isoleucyl-L-valyl-L-serylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

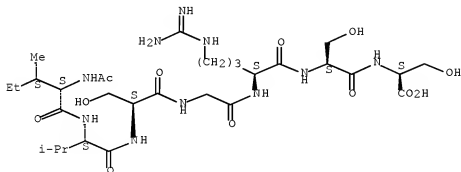
Absolute stereochemistry.



RN 642484-48-8 CAPLUS

CN L-Serine, N-acetyl-L-isoleucyl-L-valyl-L-serylglycyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

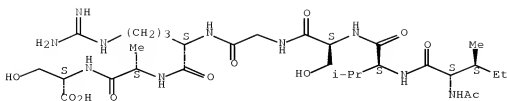
Absolute stereochemistry.



RN 642484-49-9 CAPLUS

CN L-Serine, N-acetyl-L-isoleucyl-L-valyl-L-serylglycyl-L-arginyl-L-alanyl-
(9CI) (CA INDEX NAME)

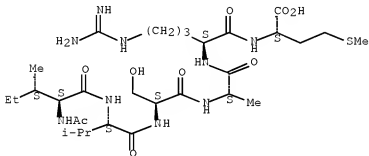
Absolute stereochemistry.



RN 642484-50-2 CAPLUS

CN L-Methionine, N-acetyl-L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl-
(9CI) (CA INDEX NAME)

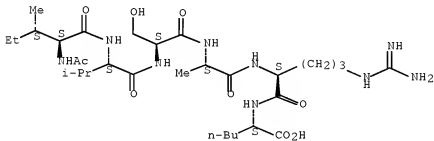
Absolute stereochemistry.



RN 642484-51-3 CAPLUS

CN L-Norleucine, N-acetyl-L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



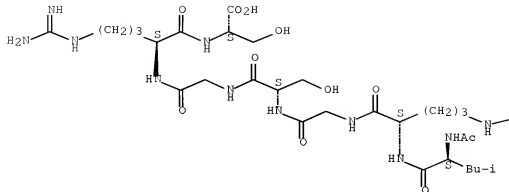
RN 642484-52-4 CAPLUS

CN L-Serine, L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

Absolute stereochemistry.

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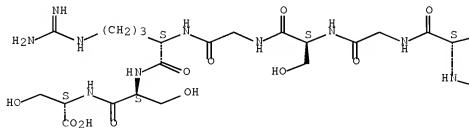


RN 642484-56-8 CAPLUS

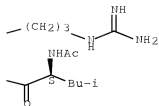
CN L-Serine, N-acetyl-L-leucyl-L-arginylglycyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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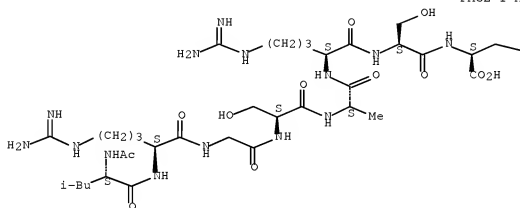


RN 642484-57-9 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginylglycyl-L-seryl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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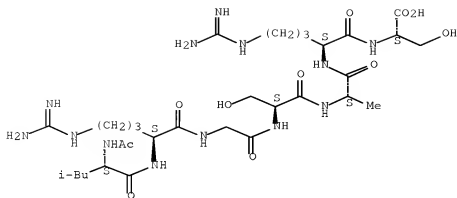
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RN 642484-58-0 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginylglycyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

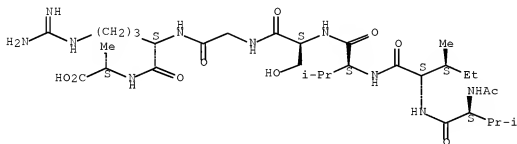
Absolute stereochemistry.



RN 642484-59-1 CAPLUS

CN L-Alanine, N-acetyl-L-valyl-L-isoleucyl-L-valyl-L-serylglycyl-L-arginyl-
(9CI) (CA INDEX NAME)

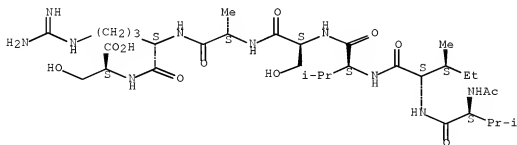
Absolute stereochemistry.



RN 642484-60-4 CAPLUS

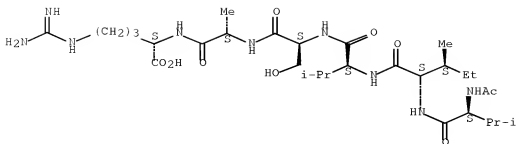
CN L-Serine, N-acetyl-L-valyl-L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 642484-61-5 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-isoleucyl-L-valyl-L-serylglycyl-L-arginyl-L-
seryl- (9CI) (CA INDEX NAME)

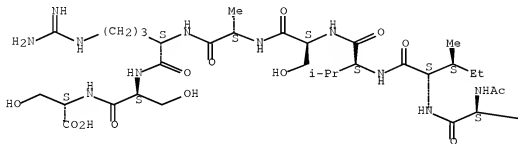


RN 642484-64-8 CAPLUS

CN L-Serine, N-acetyl-L-valyl-L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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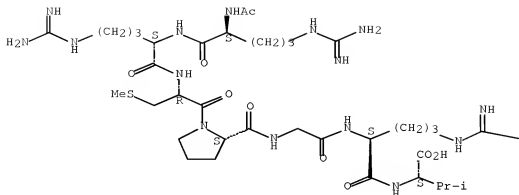
—Pr-i

RN 642484-65-9 CAPLUS

CN L-Valine, N2-acetyl-L-arginyl-L-arginyl-S-methyl-L-cysteinyl-L-prolylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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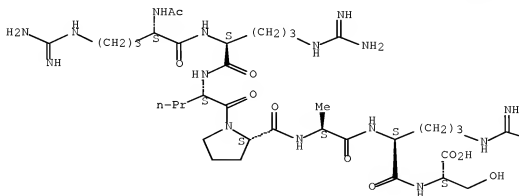
-NH2

RN 642484-66-0 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-arginyl-L-norvalyl-L-prolyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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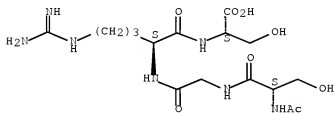
PAGE 1-B



RN 642484-67-1 CAPLUS

CN L-Serine, N-acetyl-L-serylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

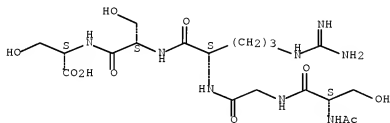
Absolute stereochemistry.



RN 642484-68-2 CAPLUS

CN L-Serine, N-acetyl-L-serylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

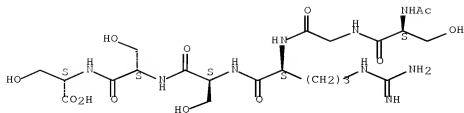
Absolute stereochemistry.



RN 642484-69-3 CAPLUS

CN L-Serine, N-acetyl-L-serylglycyl-L-arginyl-L-seryl-L-seryl- (9CI) (CA INDEX NAME)

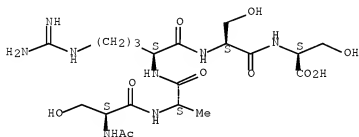
Absolute stereochemistry.



RN 642484-70-6 CAPLUS

CN L-Serine, N-acetyl-L-seryl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

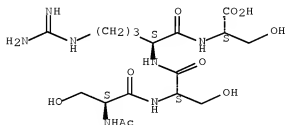
Absolute stereochemistry.



RN 642484-71-7 CAPLUS

CN L-Serine, N-acetyl-L-seryl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

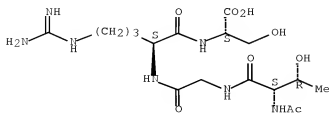
Absolute stereochemistry.



RN 642484-72-8 CAPLUS

CN L-Serine, N-acetyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

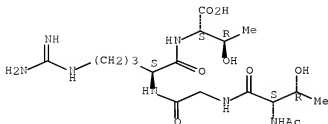
Absolute stereochemistry.



RN 642484-73-9 CAPLUS

CN L-Threonine, N-acetyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

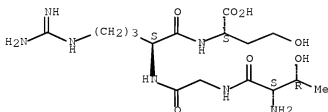
Absolute stereochemistry.



RN 642484-74-0 CAPLUS

CN L-Homoserine, L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

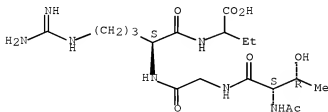
Absolute stereochemistry.



RN 642484-75-1 CAPLUS

CN Butanoic acid, N-acetyl-L-threonylglycyl-L-arginyl-2-amino- (9CI) (CA INDEX NAME)

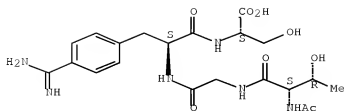
Absolute stereochemistry.



RN 642484-76-2 CAPLUS

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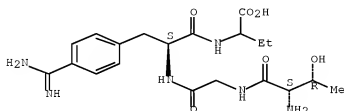
Absolute stereochemistry.



RN 642484-77-3 CAPLUS

CN Butanoic acid, L-threonylglycyl-4-(aminoiminomethyl)-L-phenylalanyl-2-amino- (9CI) (CA INDEX NAME)

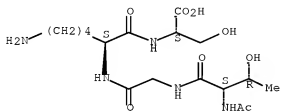
Absolute stereochemistry.



RN 642484-78-4 CAPLUS

CN L-Serine, N-acetyl-L-threonylglycyl-L-lysyl- (9CI) (CA INDEX NAME)

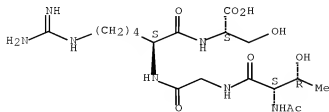
Absolute stereochemistry.



RN 642484-79-5 CAPLUS

CN L-Serine, N-acetyl-L-threonylglycyl-N6-(aminoiminomethyl)-L-lysyl- (9CI) (CA INDEX NAME)

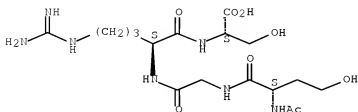
Absolute stereochemistry.



RN 642484-80-8 CAPLUS

CN L-Serine, N-acetyl-L-homoserylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

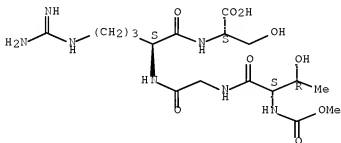
Absolute stereochemistry.



RN 642484-81-9 CAPLUS

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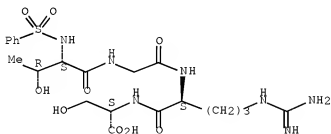
Absolute stereochemistry.



RN 642484-82-0 CAPLUS

CN L-Serine, N-(phenylsulfonyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

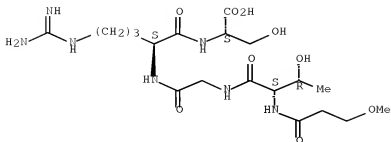
Absolute stereochemistry.



RN 642484-83-1 CAPLUS

CN L-Serine, N-(3-methoxy-1-oxopropyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

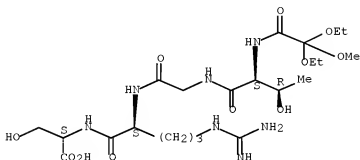
Absolute stereochemistry.



RN 642484-84-2 CAPLUS

CN L-Serine, N-(diethoxymethoxyacetyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

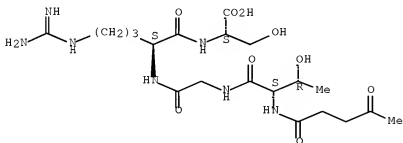
Absolute stereochemistry.



RN 642484-85-3 CAPLUS

CN L-Serine, N-(1,4-dioxopentyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

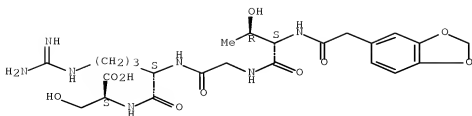
Absolute stereochemistry.



RN 642484-86-4 CAPLUS

CN L-Serine, N-(1,3-benzodioxol-5-ylacetyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

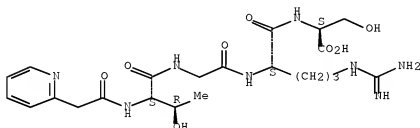
Absolute stereochemistry.



RN 642484-87-5 CAPLUS

CN L-Serine, N-(2-pyridinylacetyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

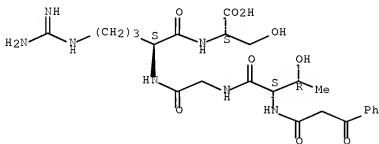
Absolute stereochemistry.



RN 642484-88-6 CAPLUS

CN L-Serine, N-(1,3-dioxo-3-phenylpropyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

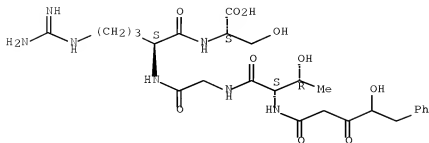
Absolute stereochemistry.



RN 642484-89-7 CAPLUS

CN L-Serine, N-(4-hydroxy-1,3-dioxo-5-phenylpentyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

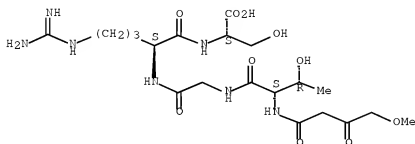
Absolute stereochemistry.



RN 642484-90-0 CAPLUS

CN L-Serine, N-(4-methoxy-1,3-dioxobutyl)-L-threonylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

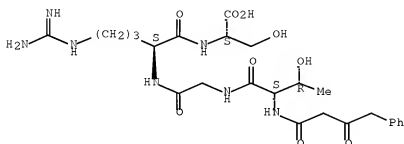
Absolute stereochemistry.



RN 642484-91-1 CAPLUS

CN L-Serine, N-(1,3-dioxo-4-phenylbutyl)-L-threonylglycyl-L-arginyl- (9CI)
(CA INDEX NAME)

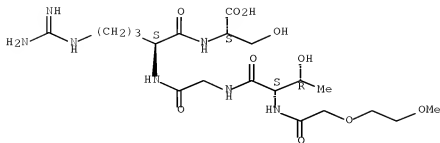
Absolute stereochemistry.



RN 642484-92-2 CAPLUS

CN L-Serine, N-[(2-methoxyethoxy)acetyl]-L-threonylglycyl-L-arginyl- (9CI)
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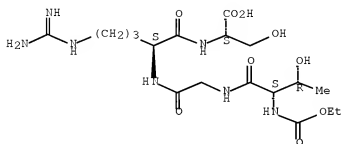
Absolute stereochemistry.



RN 642484-93-3 CAPLUS

CN L-Serine, N-(ethoxycarbonyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

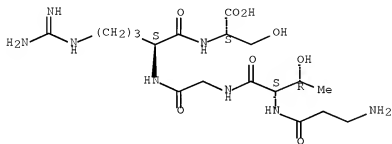
Absolute stereochemistry.



RN 642484-94-4 CAPLUS

CN L-Serine, beta-alanyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

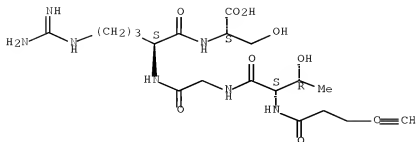
Absolute stereochemistry.



RN 642484-95-5 CAPLUS

CN L-Serine, N-(1-oxo-4-pentynyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

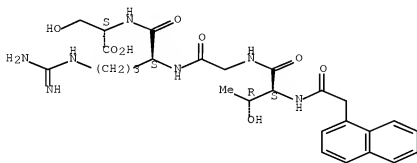
Absolute stereochemistry.



RN 642484-96-6 CAPLUS

CN L-Serine, N-(1-naphthalenylacetyl)-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

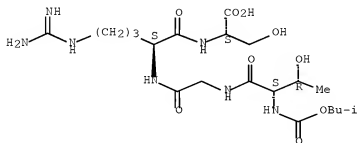
Absolute stereochemistry.



RN 642484-97-7 CAPLUS

CN L-Serine, N-[(2-methylpropoxy)carbonyl]-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

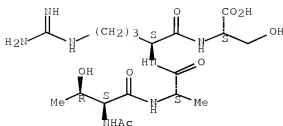
Absolute stereochemistry.



RN 642484-98-8 CAPLUS

CN L-Serine, hydroxyacetyl-L-threonylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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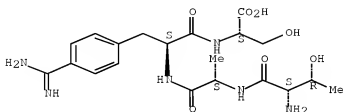
RL: BSU (Biological study, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence, as prodrug; peptide conjugates with drugs as
 prodrugs for activation by tissue or cell-specific proteinases)

RN 642485-02-7 CAPLUS

CN L-Serine, L-threonyl-L-alanyl-4-(aminoiminomethyl)-L-phenylalanyl- (9CI)
(CA INDEX NAME)

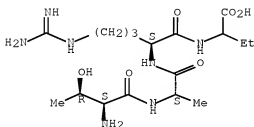
Absolute stereochemistry.



RN 642485-03-8 CAPLUS

CN Butanoic acid, L-threonyl-L-alanyl-L-arginyl-2-amino- (9CI) (CA INDEX
NAME)

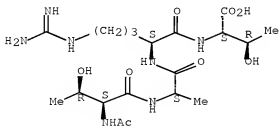
Absolute stereochemistry.



RN 642485-04-9 CAPLUS

CN L-Threonine, N-acetyl-L-threonyl-L-alanyl-L-arginyl- (9CI) (CA INDEX
NAME)

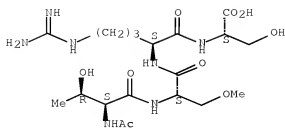
Absolute stereochemistry.



RN 642485-05-0 CAPLUS

CN L-Serine, N-acetyl-L-threonyl-O-methyl-L-seryl-L-arginyl- (9CI) (CA INDEX
NAME)

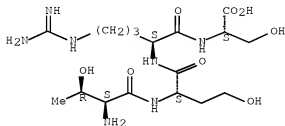
Absolute stereochemistry.



RN 642485-06-1 CAPLUS

CN L-Serine, L-threonyl-L-homoseryl-L-arginyl- (9CI) (CA INDEX NAME)

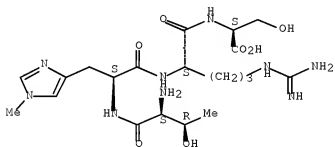
Absolute stereochemistry.



RN 642485-07-2 CAPLUS

CN L-Serine, L-threonyl-1-methyl-L-histidyl-L-arginyl- (9CI) (CA INDEX NAME)

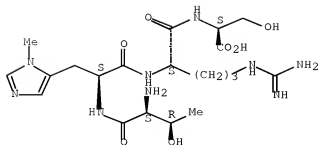
Absolute stereochemistry.



RN 642485-08-3 CAPLUS

CN L-Serine, L-threonyl-3-methyl-L-histidyl-L-arginyl- (9CI) (CA INDEX NAME)

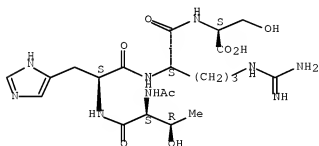
Absolute stereochemistry.



RN 642485-09-4 CAPLUS

CN L-Serine, N-acetyl-L-threonyl-L-histidyl-L-arginyl- (9CI) (CA INDEX NAME)

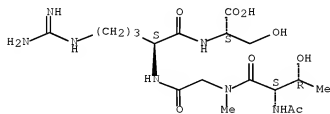
Absolute stereochemistry.



RN 642485-10-7 CAPLUS

CN L-Serine, N-acetyl-L-threonyl-N-methylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

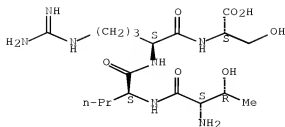
Absolute stereochemistry.



RN 642485-11-8 CAPLUS

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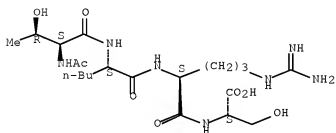
Absolute stereochemistry.



RN 642485-12-9 CAPLUS

CN L-Serine, N-acetyl-L-threonyl-L-norleucyl-L-arginyl- (9CI) (CA INDEX NAME)

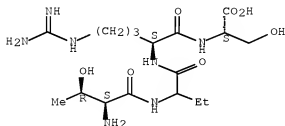
Absolute stereochemistry.



RN 642485-13-0 CAPLUS

CN L-Serine, L-threonyl-2-aminobutanoyl-L-arginyl- (9CI) (CA INDEX NAME)

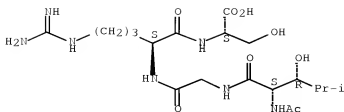
Absolute stereochemistry.



RN 642485-14-1 CAPLUS

CN L-Serine, (3R)-N-acetyl-3-hydroxy-L-leucylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

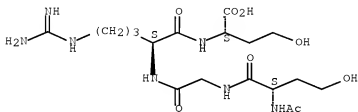
Absolute stereochemistry.



RN 642485-15-2 CAPLUS

CN L-Homoserine, N-acetyl-L-homoserylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

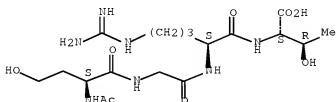
Absolute stereochemistry.



RN 642485-16-3 CAPLUS

CN L-Threonine, N-acetyl-L-homoserylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

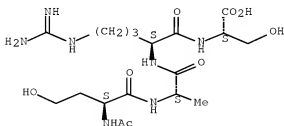
Absolute stereochemistry.



RN 642485-17-4 CAPLUS

CN L-Serine, N-acetyl-L-homoseryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

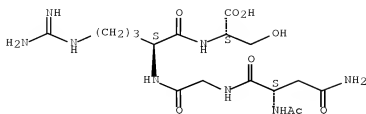
Absolute stereochemistry.



RN 642485-18-5 CAPLUS

CN L-Serine, N2-acetyl-L-asparaginyglycyl-L-arginyl- (9CI) (CA INDEX NAME)

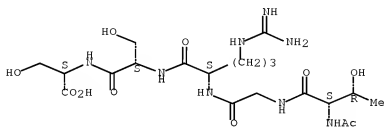
Absolute stereochemistry.



RN 642485-19-6 CAPLUS

CN L-Serine, N-acetyl-L-threonylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

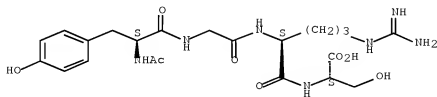
Absolute stereochemistry.



RN 642485-20-9 CAPLUS

CN L-Serine, N-acetyl-L-tyrosylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

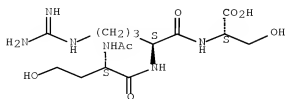
Absolute stereochemistry.



RN 642485-21-0 CAPLUS

CN L-Serine, N-acetyl-L-homoseryl-L-arginyl- (9CI) (CA INDEX NAME)

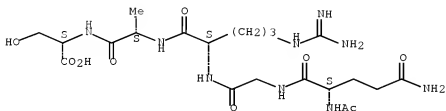
Absolute stereochemistry.



RN 642485-27-6 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminyglycyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

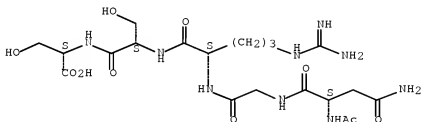
Absolute stereochemistry.



RN 642485-29-8 CAPLUS

CN L-Serine, N2-acetyl-L-asparaginyglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

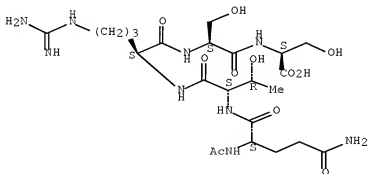
Absolute stereochemistry.



RN 642485-30-1 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminy-L-threonyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

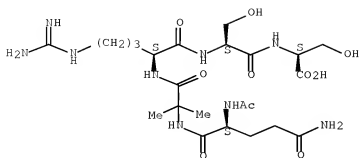
Absolute stereochemistry.



RN 642485-31-2 CAPLUS

CN L-Serine, N2-acetyl-L-glutaminy-L-2-methylalanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

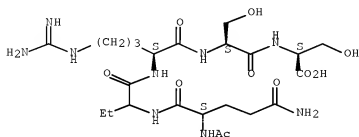
Absolute stereochemistry.



RN 642485-32-3 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-2-aminobutanoyl-L-arginyl-L-seryl- (9CI)
(CA INDEX NAME)

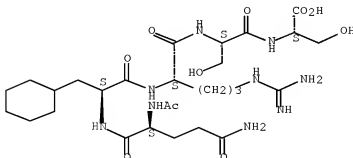
Absolute stereochemistry.



RN 642485-33-4 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-3-cyclohexyl-L-alanyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

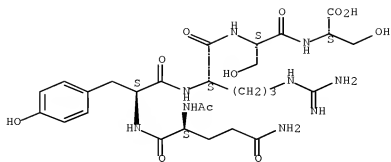
Absolute stereochemistry.



RN 642485-34-5 CAPLUS

CN L-Serine, N2-acetyl-L-glutamyl-L-tyrosyl-L-arginyl-L-seryl- (9CI) (CA
INDEX NAME)

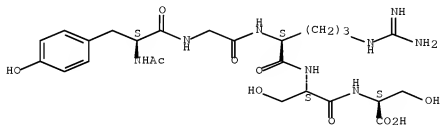
Absolute stereochemistry.



RN 642485-35-6 CAPLUS

CN L-Serine, N-acetyl-L-tyrosylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

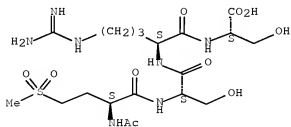
Absolute stereochemistry.



RN 642485-36-7 CAPLUS

CN L-Serine, (2S)-2-(acetylamino)-4-(methylsulfonyl)butanoyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

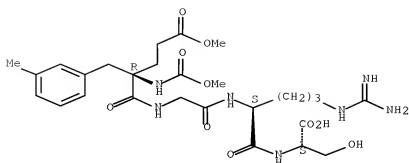
Absolute stereochemistry.



RN 642485-37-8 CAPLUS

CN L-Serine, N-(methoxycarbonyl)-2-[(3-methylphenyl)methyl]-L-alpha-glutamylglycyl-L-arginyl-, 1-methyl ester (9CI) (CA INDEX NAME)

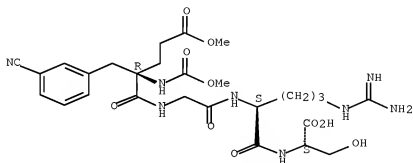
Absolute stereochemistry.



RN 642485-38-9 CAPLUS

CN L-Serine, 2-[(3-cyanophenyl)methyl]-N-(methoxycarbonyl)-L-α-glutamylglycyl-L-arginyl-, 1-methyl ester (9CI) (CA INDEX NAME)

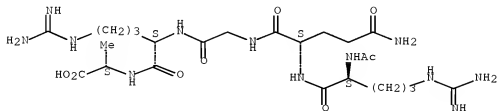
Absolute stereochemistry.



RN 642485-39-0 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-glutamylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

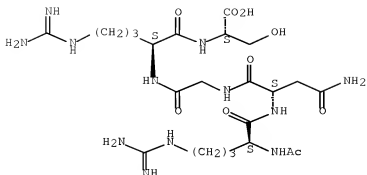
Absolute stereochemistry.



RN 642485-40-3 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-asparaginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

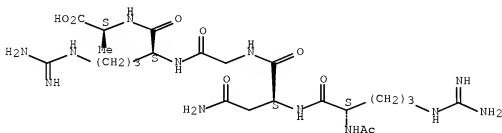
Absolute stereochemistry.



RN 642485-41-4 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-asparaginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

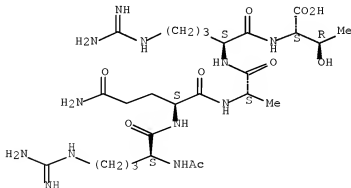
Absolute stereochemistry.



RN 642485-42-5 CAPLUS

CN L-Threonine, N2-acetyl-L-arginyl-L-glutamyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

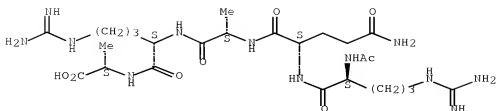
Absolute stereochemistry.



RN 642485-43-6 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-glutamyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

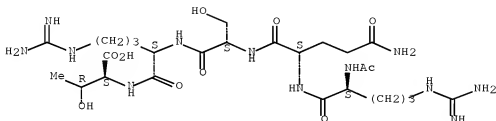
Absolute stereochemistry.



RN 642485-44-7 CAPLUS

CN L-Threonine, N2-acetyl-L-arginyl-L-glutaminyl-L-seryl-L-arginyl- (9CI)
(CA INDEX NAME)

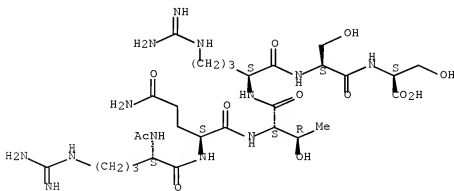
Absolute stereochemistry.



RN 642485-45-8 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyl-L-threonyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

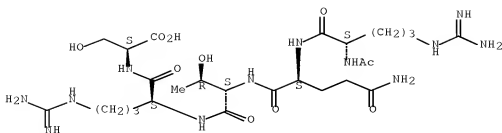
Absolute stereochemistry.



RN 642485-46-9 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-glutaminyl-L-threonyl-L-arginyl- (9CI)
(CA INDEX NAME)

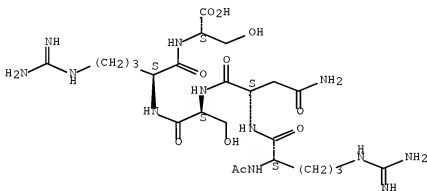
Absolute stereochemistry.



RN 642485-47-0 CAPLUS

CN L-Serine, N2-acetyl-L-arginyl-L-asparaginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

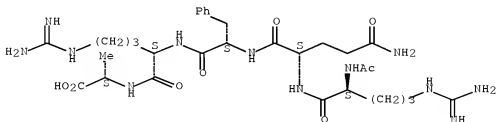
Absolute stereochemistry.



RN 642485-48-1 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-glutaminyl-L-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

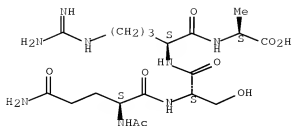
Absolute stereochemistry.



RN 642485-49-2 CAPLUS

CN L-Alanine, N2-acetyl-L-glutaminyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

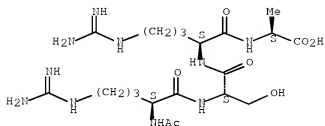
Absolute stereochemistry.



RN 642485-50-5 CAPLUS

CN L-Alanine, N2-acetyl-L-arginyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

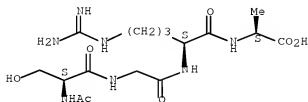
Absolute stereochemistry.



RN 642485-52-7 CAPLUS

CN L-Alanine, N-acetyl-L-serylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

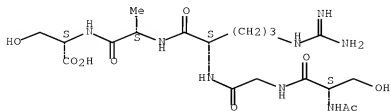
Absolute stereochemistry.



RN 642485-53-8 CAPLUS

CN L-Serine, N-acetyl-L-serylglycyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

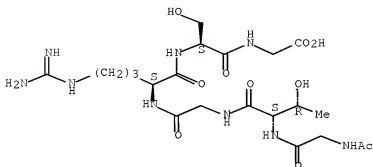
Absolute stereochemistry.



RN 642485-54-9 CAPLUS

CN Glycine, N-acetylglycyl-L-threonylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

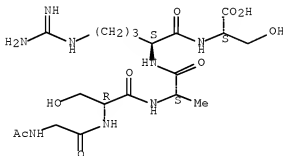
Absolute stereochemistry.



RN 642485-55-0 CAPLUS

CN L-Serine, N-acetylglycyl-D-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

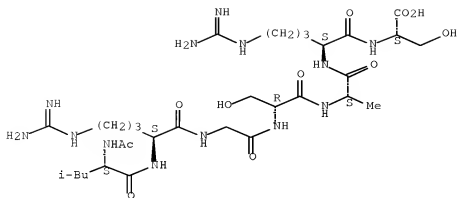
Absolute stereochemistry.



RN 642485-56-1 CAPLUS

CN L-Serine, N-acetyl-L-leucyl-L-arginylglycyl-D-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

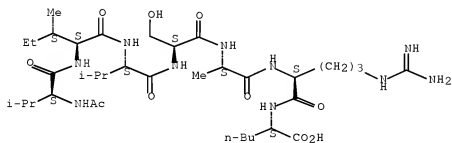
Absolute stereochemistry.



RN 642485-57-2 CAPLUS

CN L-Norleucine, N-acetyl-L-valyl-L-isoleucyl-L-valyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

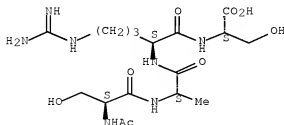
Absolute stereochemistry.



RN 642485-58-3 CAPLUS

CN L-Serine, N-acetyl-L-seryl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

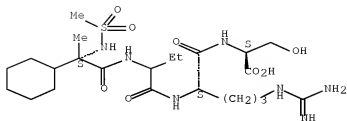
Absolute stereochemistry.



RN 642485-59-4 CAPLUS

CN L-Serine, 2-cyclohexyl-N-(methylsulfonyl)-D-alanyl-2-aminobutanoyl-L-arginyl- (9CI) (CA INDEX NAME)

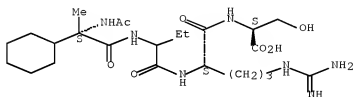
Absolute stereochemistry.



RN 642485-60-7 CAPLUS

CN L-Serine, N-acetyl-2-cyclohexyl-D-alanyl-2-aminobutanoyl-L-arginyl- (9CI)
(CA INDEX NAME)

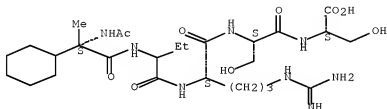
Absolute stereochemistry.



RN 642485-61-8 CAPLUS

CN L-Serine, N-acetyl-2-cyclohexyl-D-alanyl-2-aminobutanoyl-L-arginyl-L-seryl-
(9CI) (CA INDEX NAME)

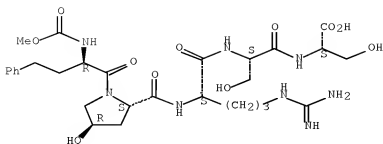
Absolute stereochemistry.



RN 642485-62-9 CAPLUS

CN L-Serine, (alphaR)-alpha-[(methoxycarbonyl)amino]benzenebutanoyl-(4R)-
4-hydroxy-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

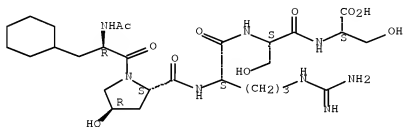
Absolute stereochemistry.



RN 642485-63-0 CAPLUS

CN L-Serine, N-acetyl-3-cyclohexyl-D-alanyl-(4R)-4-hydroxy-L-prolyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

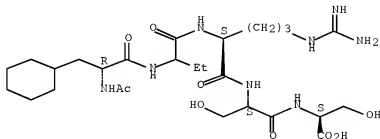
Absolute stereochemistry.



RN 642485-64-1 CAPLUS

CN L-Serine, N-acetyl-3-cyclohexyl-D-alanyl-2-aminobutanoyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

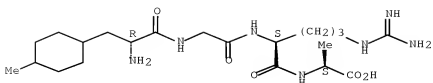
Absolute stereochemistry.



RN 642928-58-3 CAPLUS

CN L-Alanine, 3-(4-methylcyclohexyl)-D-alanylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

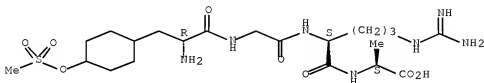
Absolute stereochemistry.



RN 642928-61-8 CAPLUS

CN L-Alanine, 3-[4-(methylsulfonyl)oxycyclohexyl]-D-alanylglycyl-L-arginyl-
(9CI) (CA INDEX NAME)

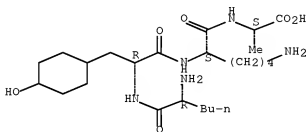
Absolute stereochemistry.



RN 642928-64-1 CAPLUS

CN L-Alanine, D-norleucyl-3-(4-hydroxycyclohexyl)-D-alanyl-L-lysyl- (9CI)
(CA INDEX NAME)

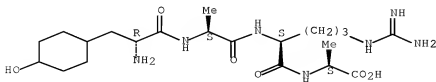
Absolute stereochemistry.



RN 642928-67-4 CAPLUS

CN L-Alanine, 3-(4-hydroxycyclohexyl)-D-alanyl-L-alanyl-L-arginyl- (9CI) (CA
INDEX NAME)

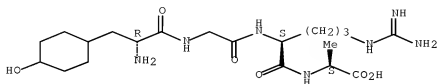
Absolute stereochemistry.



RN 642928-70-9 CAPLUS

CN L-Alanine, 3-(4-hydroxycyclohexyl)-D-alanylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

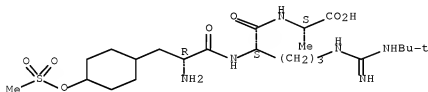
Absolute stereochemistry.



RN 642928-73-2 CAPLUS

CN L-Alanine, 3-[4-[(methylsulfonyl)oxycyclohexyl]-D-alanyl-N5-[[1,1-dimethylethyl)amino]iminomethyl]-L-ornithyl- (9CI) (CA INDEX NAME)

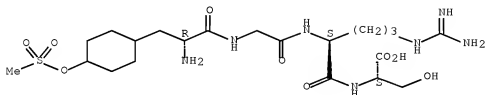
Absolute stereochemistry.



RN 642928-76-5 CAPLUS

CN L-Serine, 3-[4-[(methylsulfonyl)oxycyclohexyl]-D-alanylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

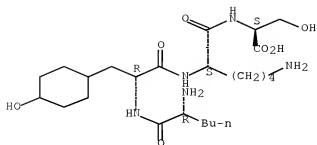
Absolute stereochemistry.



RN 642928-79-8 CAPLUS

CN L-Serine, D-norleucyl-3-(4-hydroxycyclohexyl)-D-alanyl-L-lysyl- (9CI) (CA INDEX NAME)

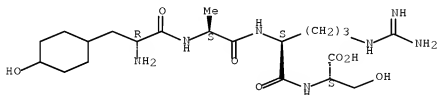
Absolute stereochemistry.



RN 642928-81-2 CAPLUS

CN L-Serine, 3-(4-hydroxycyclohexyl)-D-alanyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

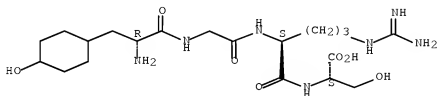
Absolute stereochemistry.



RN 642928-83-4 CAPLUS

CN L-Serine, 3-(4-hydroxycyclohexyl)-D-alanylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

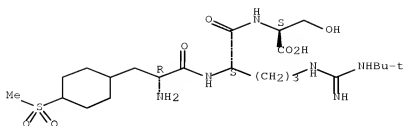
Absolute stereochemistry.



RN 642928-85-6 CAPLUS

CN L-Serine, 3-[4-(methylsulfonyl)cyclohexyl]-D-alanyl-N5-[[[(1,1-dimethylethyl)amino]iminomethyl]-L-ornithyl- (9CI) (CA INDEX NAME)

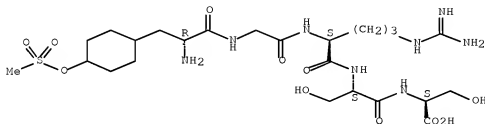
Absolute stereochemistry.



RN 642928-87-8 CAPLUS

CN L-Serine, 3-[4-[(methylsulfonyl)oxy]cyclohexyl]-D-alanylglycyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

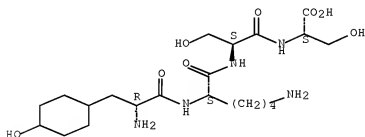
Absolute stereochemistry.



RN 642928-90-3 CAPLUS

CN L-Serine, 3-(4-hydroxycyclohexyl)-D-alanyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

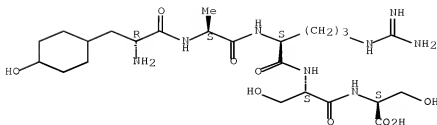
Absolute stereochemistry.



RN 642928-92-5 CAPLUS

CN L-Serine, 3-(4-hydroxycyclohexyl)-D-alanyl-L-alanyl-L-arginyl-L-seryl- (9CI) (CA INDEX NAME)

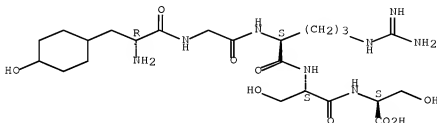
Absolute stereochemistry.



RN 642928-94-7 CAPLUS

CN L-Serine, 3-(4-hydroxycyclohexyl)-D-alanylglycyl-L-arginyl-L-seryl- (9CI)
(CA INDEX NAME)

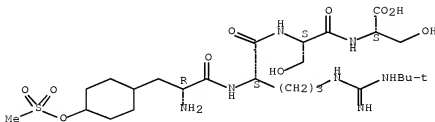
Absolute stereochemistry.



RN 642928-96-9 CAPLUS

CN L-Serine, 3-[4-[(methylsulfonyl)oxy]cyclohexyl]-D-alanyl-N5-[[[1,1-dimethylethyl]amino]iminomethyl]-L-ornithyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 2003:833884 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:317425

TITLE: Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis

INVENTOR(S): Debatin, Klaus Michael; Fulda, Simone
PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung des Oeffentlichen Rechts, Germany

SOURCE: Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354952	A1	20031022	EP 2002-8199	20020417 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1354953	A1	20031022	EP 2002-15499	20020712 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2003086470	A2	20031023	WO 2003-EP4039	20030417 <--
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003236211	A1	20031027	AU 2003-236211	20030417 <--
EP 1495124	A2	20050112	EP 2003-722503	20030417 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005536457	T	20051202	JP 2003-583486	20030417 <--
US 2005022387	A1	20051006	US 2005-511037	20050119 <--
PRIORITY APPLN. INFO.:			EP 2002-8199	A 20020417 <--
			EP 2002-15499	A 20020712 <--
			WO 2003-EP4039	W 20030417

AB The invention is directed to the use of Smac to sensitize different tumors and self-reactive immune cells to various pro-apoptotic stimuli, in that the cells subsequently undergo apoptosis. Therefore, Smac can be used as a compound for the manufacture of a medicament for the treatment of cancer and autoimmune diseases. Sensitization of the cells is achieved either by applying a cell-permeable form of Smac combined with known anticancer agents or by overexpression of the protein. It is an object of the invention to provide a new method in cancer and autoimmune disease therapy by using Smac agonists for apoptosis regulation. Thus, Smac agonists represent novel promising cancer and autoimmune disease therapeutics to potentiate the efficacy of cytotoxic therapies even in resistant tumors and immune cells. In particular, overexpression of full-length Smac protein potentiated TRAIL-induced apoptosis and also markedly increased apoptosis induced by anti-CD95 antibody or cytotoxic drugs in transfected SHEP neuroblastoma cells. The overexpression of Smac is shown to promote apoptosis through antagonizing the inhibition of XIAP of both distal and proximal events in the caspase cascade. The cytosolic Smac, with the deletion of transit peptide for mitochondria (N-terminal 55 AA), bypasses Bcl-2 inhibition in several cell types in response to different pro-apoptotic stimuli. The cell permeable Smac peptide (4 N-terminal IAP-interacting plus 3 additional following residues linked to TAT transduction domain) can facilitate intracellular delivery of Smac peptide and sensitize several resistant cell lines with defects in apoptosis signaling for treatment with TRAIL or doxorubicin. Expression of a cytosolic active form of Smac or cell-permeable Smac peptides bypassed the Bcl-2 block, which prevented the release of Smac from mitochondria, and also sensitized resistant neuroblastoma or melanoma cells and patient-derived primary neuroblastoma cells *ex vivo*.

Thus, Smac agonists represent novel promising cancer therapeutics to potentiate the efficacy of cytotoxic therapies. Smac peptides is shown to enhance the antitumor effect of TRAIL in glioblastoma in mouse glioblastoma model and induce eradication of tumors.

- IC ICM C12N015-12
ICS C12N015-62; A61K047-48; C07K005-103; C07K019-00; C07K014-47; A61K038-17
- CC 1-6 (Pharmacology)
Section cross-reference(s): 6, 13, 15, 63
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2, drug resistant cancer cell line overexpressing;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Bone, neoplasm
(Ewing's sarcoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Antirheumatic agents
Antitumor agents
Autoimmune disease
Gene therapy
Genetic engineering
Human
Human herpesvirus
Human immunodeficiency virus 1
Influenza virus
Neoplasm
(Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Uterus, neoplasm
(adenocarcinoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Drug resistance
(antitumor, treatment of cancers with; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Neuroglia, neoplasm
(astrocytoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Skin, neoplasm
(basal cell carcinoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Stomach, neoplasm
(carcinoma, carcinoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Bladder, neoplasm
Bronchi, neoplasm
Esophagus, neoplasm
Gallbladder, neoplasm
Larynx, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Salivary gland, neoplasm

- Testis, neoplasm
 Tongue, neoplasm
 (carcinoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Uterus, neoplasm
 (cervix, carcinoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Cartilage, neoplasm
 (chondrosarcoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Carcinoma
 Chorion, neoplasm
 (choriocarcinoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Intestine, neoplasm
 (colon, carcinoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Carcinoma
 Intestine, neoplasm
 (colon, treatment using SMAC peptide combinatory drugs; Smac-peptides
 as therapeutics against cancer and autoimmune diseases by sensitizing
 for TRAIL- or anticancer drug-induced apoptosis)
- IT Intestine, neoplasm
 (colorectal hereditary nonpolyposis carcinoma, familial adenomatous
 polyposis carcinoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Pituitary gland, neoplasm
 (craniopharyngeoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Microtubule
 (directed agents, therapeutic combination with SMAC peptide;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Uterus, neoplasm
 (endometrium, carcinoma, treatment using SMAC peptide combinatory
 drugs; Smac-peptides as therapeutics against cancer and autoimmune
 diseases by sensitizing for TRAIL- or anticancer drug-induced
 apoptosis)
- IT Neuroglia, neoplasm
 (glioblastoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Liver, neoplasm
 (hepatoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Adipose tissue, neoplasm
 Sarcoma
 (liposarcoma, treatment using SMAC peptide combinatory drugs;
 Smac-peptides as therapeutics against cancer and autoimmune diseases by
 sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Thyroid gland, neoplasm
 (medullary carcinoma, carcinoma, treatment using SMAC peptide

- combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Brain, neoplasm
(medulloblastoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Nervous system, neoplasm
(meningioma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Nerve, neoplasm
(neuroblastoma, disease model; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Nerve, neoplasm
(neuroblastoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Nervous system, neoplasm
(neuroectoderm, peripheral, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Lung, neoplasm
(non-small-cell carcinoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Bone, neoplasm
Sarcoma
(osteosarcoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Thyroid gland, neoplasm
(papillary carcinoma, carcinoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Intestine, neoplasm
(rectum, carcinoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Kidney, neoplasm
(renal cell carcinoma, parenchym carcinoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Kidney, neoplasm
(renal cell carcinoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Antitumor agents
(resistance to, treatment of cancers with; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Eye, neoplasm
(retinoblastoma, treatment using SMAC peptide combinatory drugs; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

- IT Testis, neoplasm
(seminoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by
sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Lung, neoplasm
(small-cell carcinoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by
sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT Pharynx, neoplasm
(squamous cell carcinoma, treatment using SMAC peptide combinatory
drugs; Smac-peptides as therapeutics against cancer and autoimmune
diseases by sensitizing for TRAIL- or anticancer drug-induced
apoptosis)
- IT Neoplasm
(teratoma, treatment using SMAC peptide combinatory drugs;
Smac-peptides as therapeutics against cancer and autoimmune diseases by
sensitizing for TRAIL- or anticancer drug-induced apoptosis)
- IT AIDS (disease)
Acute lymphocytic leukemia
Acute myeloid leukemia
Addison's disease
Adult T-cell leukemia
Blood, disease
Brain, neoplasm
Chronic lymphocytic leukemia
Chronic myeloid leukemia
Connective tissue, disease
Dermatomyositis
Hodgkin's disease
Hyperthyroidism
Infection
Liver, disease
Malaria
Melanoma
Multiple myeloma
Multiple sclerosis
Myasthenia gravis
Nervous system, disease
Prostate gland, neoplasm
Rheumatoid arthritis
Skin, disease
(treatment using SMAC peptide combinatory drugs; Smac-peptides as
therapeutics against cancer and autoimmune diseases by sensitizing for
TRAIL- or anticancer drug-induced apoptosis)
- IT 155893-31-5 612883-04-2
RL: BUU (Biological use, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV1 transduction domain peptide; Smac-peptides as therapeutics
against cancer and autoimmune diseases by sensitizing for TRAIL- or
anticancer drug-induced apoptosis)
- IT 401913-54-0P 401913-57-3P 612824-52-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PAC (Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(SMAC IAP-interacting peptide; Smac-peptides as therapeutics against
cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer
drug-induced apoptosis)
- IT 395969-86-0P, Pep-1, fusion product with SMAC peptide
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)

(Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

IT 24937-47-1, Polyarginine 62031-54-3, Fibroblast growth factor 179352-81-7, Galparan

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(fusion product with SMAC peptide; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

IT 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, FdUrd 51-21-8, Fluorouracil 52-24-4, Thiotepa 52-76-6, Lynestrenol 53-79-2, Puromycin 55-86-7, Nitrogen mustard 55-98-1, Busulfan 57-22-7, Vincristine 57-63-6, Ethinylestradiol 58-22-0, Testosterone 59-05-2, Methotrexate 59-30-3D, Folic acid, analogs 64-86-8, Colchicine 66-81-9, Cycloheximide 68-22-4, Norethisterone 79-81-2, Retinopalmitate 117-39-5, Quercetin 120-73-0D, Purine, analogs 125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3 154-42-7D, Tioguanine, analogs 154-93-8, Carmustine 289-95-2D, Pyrimidine, analogs 299-75-2, Treosulfan 302-79-4, Tretinoin 305-03-3, Chlorambucil 472-15-1, Betulinic acid 477-30-5, Colcemid 501-36-0, Resveratrol 518-28-5, Podophyllotoxin 520-85-4, Medroxyprogesterone 522-40-7, Fosfestrol 566-48-3, Formestane 671-16-9, Procarbazine 865-21-4, Vinblastine 968-93-4, Testolactone 970-74-1 1253-28-7, Gestonorone caproate 1492-18-8, Calciumfolinate 2098-66-0, Cyproterone 2998-57-4, Estramustine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 4346-18-3, Phenyl butyrate 4670-05-7, Theaflavin 7689-03-4, Camptothecin 9015-68-3, L-Asparaginase 10083-24-6, Piceatannol 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 15663-27-1, Cisplatin 16506-27-7, Bendamustine 19767-45-4, Mesna 19965-15-2, Thioplatin 20537-88-6, Amifostine 20830-81-3, Daunorubicine 21679-14-1, Fludarabine 22089-22-1, Trofosfamide 25316-40-9, Adriamycin 31292-79-2 31441-78-8, Mercaptopurine 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 42471-28-3, Nimustine 42615-49-6, Amlomer 53643-48-4, Vindesine 53714-56-0, Leuporelin 53910-25-1, Pentostatin 56420-45-2, Epirubicin 57576-44-0, Acliarubicin 57773-63-4, Triptoreline 57982-77-1, Buserelin 58066-85-6, Miltefosine 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 62996-74-1, Staurosporin 65271-80-9, Mitoxantrone 65646-68-6, Fenretinide 55807-02-5, Goserelin 70641-51-9, ET-18-OCN3 71486-22-1, Vinorelbine 73459-61-7, Polyestradiol 74707-94-1, Mitomycin 77286-66-9, ET 18-OCN3 85622-93-1, Temozolomide 89778-26-7 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 98319-26-7, Finasteride 99283-10-0, Molgramostim 110942-02-4, Aldesleukin 112809-51-5, Letrozole 112953-11-4, UCN-01 114977-28-5, Docetaxel 121181-53-1, Filgrastim 123948-87-8, Topotecan 130167-69-0, Pegaspargase 135968-09-1, Lenograstim 146426-40-6, Flavopiridol 156511-34-1, L 739749 160141-09-3, L-744832 174722-31-7, Rituximab 179324-69-7, PS-341 180288-69-1, Trastuzumab 220127-57-1, STI571

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(therapeutic combination with SMAC peptide; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

IT 155893-31-5

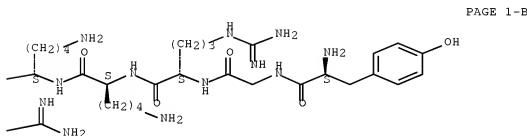
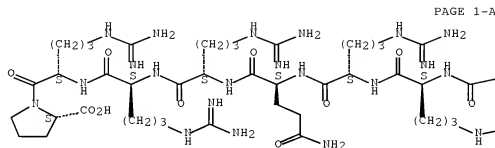
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HIV1 transduction domain peptide; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

RN 155893-31-5 CAPLUS

CN L-Proline, L-tyrosylglycyl-L-arginyl-L-lysyl-L-lysyl-L-arginyl-L-arginyl-L-glutaminy-L-arginyl-L-arginyl-L-arginyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 401913-57-3P 612824-52-9P

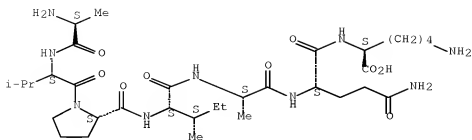
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(SMAC IAP-interacting peptide; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

RN 401913-57-3 CAPLUS

CN L-Lysine, L-alanyl-L-valyl-L-prolyl-L-isoleucyl-L-alanyl-L-glutaminy-L- (CA INDEX NAME)

Absolute stereochemistry.

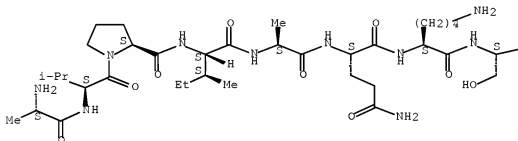


RN 612824-52-9 CAPLUS

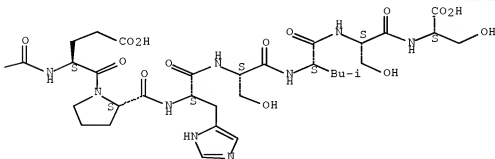
CN L-Serine, L-alanyl-L-valyl-L-prolyl-L-isoleucyl-L-alanyl-L-glutamyl-L-lysyl-L-seryl-L- α -glutamyl-L-prolyl-L-histidyl-L-seryl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 395069-86-0D, Pep-1, fusion product with SMAC peptide

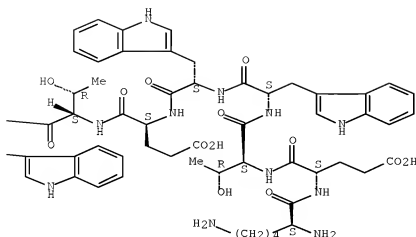
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

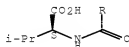
RN 395069-86-0 CAPLUS

CN L-Valine, L-lysyl-L- α -glutamyl-L-threonyl-L-tryptophyl-L-tryptophyl-

PAGE 1-C



PAGE 2-A



IT 177352-81-7, Galparan

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

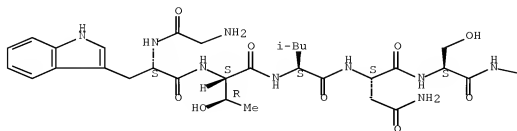
(fusion product with SMAC peptide; Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis)

RN 177352-81-7 CAPLUS

CN L-Leucinamide, glycyl-L-tryptophyl-L-threonyl-L-leucyl-L-asparaginyl-L-seryl-L-alanylglycyl-L-tyrosyl-L-leucyl-L-leucylglycyl-L-prolyl-L-isoleucyl-L-asparaginyl-L-leucyl-L-lysyl-L-alanyl-L-leucyl-L-alanyl-L-alanyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



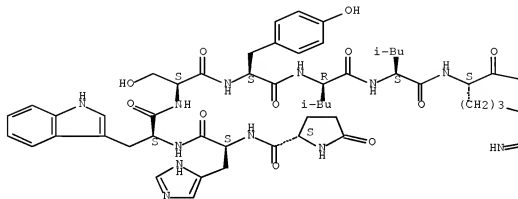
TRAIL- or anticancer drug-induced apoptosis)

RN 53714-56-0 CAPLUS

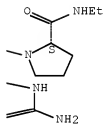
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

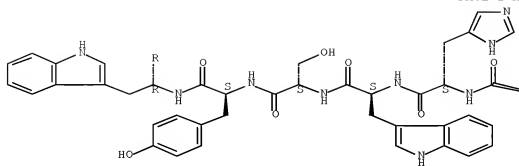


RN 57773-63-4 CAPLUS

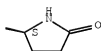
CN Luteinizing hormone-releasing factor (swine), 6-D-tryptophan- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

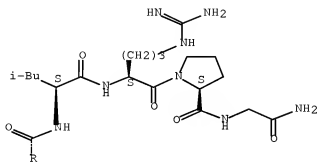
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PAGE 1-B



PAGE 2-A

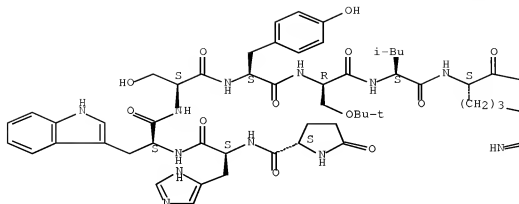


RN 57982-77-1 CAPLUS

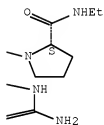
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

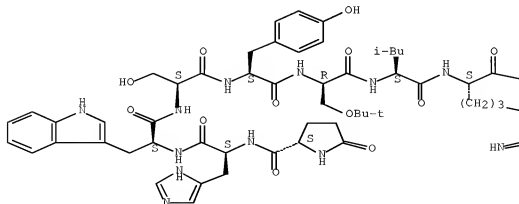


RN 65807-02-5 CAPLUS

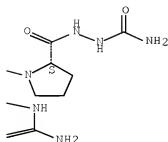
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2003:644470 CAPLUS Full-text

DOCUMENT NUMBER: 139:196272

TITLE: Antibody specific to fragment of human reticulocalbin-1 for monitoring resistance of antitumor agent

INVENTOR(S): Maeda, Masahiro; Takekawa, Kozo; Hamada, Katsumi; Hamanaka, Kozue; Ohira, Tatsuo; Hirano, Takashi; Kato, Harufumi

PATENT ASSIGNEE(S): Meneki Seibutsu Kenkyusho K. K., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003231700	A	20030819	JP 2002-28617	20020205 <--
PRIORITY APPLN. INFO.:			JP 2002-28617	20020205 <--

AB Provided is a monoclonal antibody specific to N-terminal peptide sequence of human reticulocalbin-1. Human reticulocalbin-1 is a useful marker for drug (or antitumor agent) resistance. The antibody is especially useful for monitoring the effectiveness or resistance occurrence of chemotherapeutic agent against human primary lung cancer.

IC ICM C07K016-32
ICS G01N033-53; C12N015-09

CC 15-3 (Immunochimistry)
Section cross-reference(s): 3, 9

IT Antitumor agents
Biomarkers
Chemotherapy
Drug resistance
Human
Lung, neoplasm
Molecular cloning
Protein motifs
Protein sequences

(monoclonal antibody specific to fragment of human reticulocalbin-1 for monitoring resistance of antitumor or chemotherapeutic agent against human primary lung cancer)

IT 581798-20-1 581798-21-2

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal antibody specific to fragment of human reticulocalbin-1 for monitoring resistance of antitumor or chemotherapeutic agent against human primary lung cancer)

IT 581798-20-1 581798-21-2

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

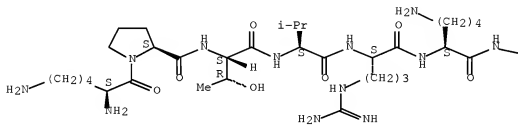
(monoclonal antibody specific to fragment of human reticulocalbin-1 for monitoring resistance of antitumor or chemotherapeutic agent against human primary lung cancer)

RN 581798-20-1 CAPLUS

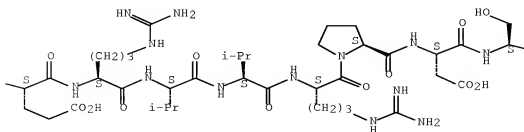
CN L-Glutamic acid, L-lysyl-L-prolyl-L-threonyl-L-valyl-L-arginyl-L-lysyl-L- α -glutamyl-L-arginyl-L-valyl-L-valyl-L-arginyl-L-prolyl-L- α -aspartyl-L-seryl-L- α -glutamyl-L-leucylglycyl-L- α -glutamyl-L-arginyl-L-prolyl-L-prolyl- (9CI) (CA INDEX NAME)

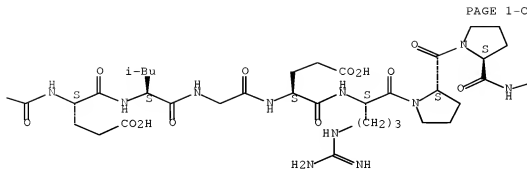
Absolute stereochemistry.

PAGE 1-A

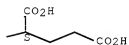


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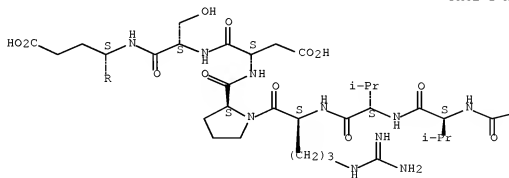


RN 581798-21-2 CAPLUS

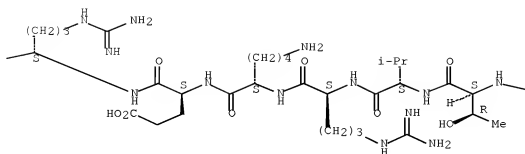
CN L-Cysteine, L-lysyl-L-prolyl-L-threonyl-L-valyl-L-arginyl-L-lysyl-L-
 α -glutamyl-L-arginyl-L-valyl-L-valyl-L-arginyl-L-prolyl-L- α -
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Absolute stereochemistry.

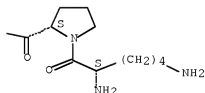
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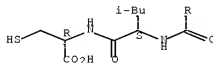
PAGE 1-B



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L80 ANSWER 9 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:591309 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:128005

TITLE: Polynucleotides and polypeptides useful in screening compounds interacting with protein tyrosine kinases and/or protein tyrosine kinase pathways in drug-sensitive and drug-resistant colon cells
 Huang, Fei; Fairchild, Craig R.; Lee, Francis Y.; Shaw, Peter

INVENTOR(S):

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 139 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062395	A2	20030731	WO 2003-US1981	20030117 <--
WO 2003062395	A3	20050407		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003209340	A1	20030902	AU 2003-209340	20030117 <--
EP 1534739	A2	20050601	EP 2003-707494	20030117 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005523688	T	20050811	JP 2003-562263	20030117 <--
US 20070166704	A1	20070719	US 2003-348119	20030117 <--
US 20060046249	A1	20060302	US 2005-501035	20050502 <--
PRIORITY APPLN. INFO.:			US 2002-350061P	P 20020118 <--
			WO 2003-US1981	W 20030117

AB The present invention describes polynucleotides and polypeptides that have been discovered to correlate to the relative intrinsic sensitivity or resistance of cells, e.g., colon cell lines, to treatment with compds. that interact with and inhibit src tyrosine kinases. These polynucleotides and polypeptides have been shown, through a weighted voting cross-validation program, to have utility in predicting the intrinsic resistance and sensitivity of colon cell lines to these compds. Oligonucleotide microarrays (the Affymetrix HG-U95Av2 array) were utilized to measure the expression levels of >12,000 polynucleotides and polypeptides in a panel of 31 untreated colon cell lines for which the drug sensitivity to four src kinase inhibitor compds. (BMS-A, BMS-B, BMS-C, BMS-D) was determined using an in vitro cytotoxicity assay to determination IC50. Such polynucleotides and polypeptides whose expression levels correlate highly with drug sensitivity or resistance comprise predictor or marker sets of polynucleotides and polypeptides that are useful in methods of predicting drug response and as prognostic or diagnostic indicators in disease management, particularly in those disease areas in which signaling through src tyrosine kinase of the src tyrosine kinase pathway is involved with the disease process.

IC ICM C12N

CC 1-6 (Pharmacology)

IT Intestine

Intestine, neoplasm

(colon); polynucleotides and polypeptides useful in screening compds. interacting with protein tyrosine kinases and/or protein tyrosine kinase pathways in drug-sensitive and drug-resistant colon cells)

IT Antitumor agents

Cytotoxicity

Drug resistance

Drug screening

Human

(polynucleotides and polypeptides useful in screening compds.
interacting with protein tyrosine kinases and/or protein tyrosine
kinase pathways in drug-sensitive and drug-resistant colon cells)

IT 568556-16-1 568609-08-5 568609-09-6 568609-10-9
568609-11-0 568609-12-1 568609-13-2 568609-14-3 568609-15-4
568609-16-5 568609-17-6 568609-18-7 568609-19-8 568609-20-1
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568610-91-3 568610-92-4 568610-93-5

RL: ARU (Analytical role, unclassified); BSU (Biological study,
unclassified); THU (Therapeutic use); ANST (Analytical study);
BIOL (Biological study); USES (Uses)

(amino acid sequence; polynucleotides and polypeptides useful in
screening compds. interacting with protein tyrosine kinases and/or
protein tyrosine kinase pathways in drug-sensitive and drug-
resistant colon cells)

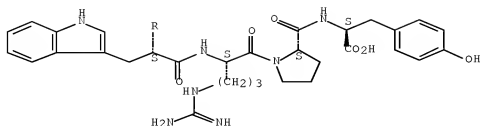
IT 568556-16-1
RL: ARU (Analytical role, unclassified); BSU (Biological study,
unclassified); THU (Therapeutic use); ANST (Analytical study);
BIOL (Biological study); USES (Uses)
(amino acid sequence; polynucleotides and polypeptides useful in
screening compds. interacting with protein tyrosine kinases and/or
protein tyrosine kinase pathways in drug-sensitive and drug-
resistant colon cells)

RN 568556-16-1 CAPLUS

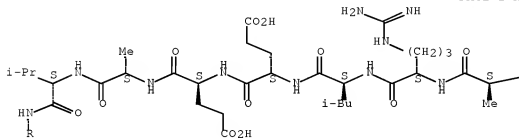
CN L-Tyrosine, L-alanyl-L-prolyl-L-seryl-L-alanyl-L-arginyl-L-leucyl-L-
α-glutamyl-L-α-glutamyl-L-alanyl-L-valyl-L-tryptophyl-L-
arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

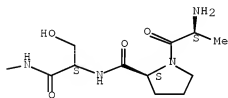
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PAGE 2-B



L80 ANSWER 10 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:524032 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:79130

TITLE: Use of 5'-substituted nucleosides for prevention of drug resistance in cytostatic treatment, and drug containing these nucleosides, polymers, methods of use, and compositions

INVENTOR(S): Fahrig, Rudolf; Steinkamp-Zucht, Angela

PATENT ASSIGNEE(S): Resprotect GmbH, Germany

SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 875,491, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6589941	B1	20030708	US 2000-520901	20000307 <--
DE 19545892	A1	19970612	DE 1995-19545892	19951208 <--
WO 9623506	A1	19960808	WO 1996-DE169	19960131 <--

W: BR, JP, KR, MX, NO, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:
DE 1995-19503152 A 19950201 <--
DE 1995-19545892 A 19951208 <--
WO 1996-DE169 B2 19960131 <--
US 1997-875491 B2 19971014 <--

AB The invention relates to a method of producing a composition and to a composition for preventing or reducing formation of resistance in cytostatic treatment comprising combining BVDU, a salt thereof or BVDU in protected form or in prodrug form, with at least one cytostatic agent in order to prevent or reduce the formation of resistance during cytostatic treatment. The present invention is also directed to a method of reducing resistance in cytostatic treatment comprising delivering therapeutically-effective amount of at least one cytostatic agent and a therapeutically effective amount of BVDU, a salt thereof, or BVDU in protected form or in prodrug form.

IC ICM A01N043-04
ICS A61K031-70

INCL 514050000; 514051000; 514052000; 514974000

CC 1-6 (Pharmacology)
Section cross-reference(s): 2, 15, 63

IT Antitumor agents
(antibiotic; substituted nucleosides for prevention of drug resistance in cytostatic treatment)

IT Antitumor agents
(resistance to; substituted nucleosides for prevention of drug resistance in cytostatic treatment)

IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-76-0, Dactinomycin 53-19-0, Mitotane 54-42-2, 5-Iodo-2'-deoxyuridine 54-71-7, Pilocarpine hydrochloride 55-86-7, Mechlorethamine hydrochloride 55-98-1, Busulfan 58-05-9, Leucovorin 58-18-4, Methyltestosterone 70-00-8, 2'-Deoxy-5-trifluoromethyluridine 71-58-9, Medroxyprogesterone acetate 125-02-0, Prednisolone sodium phosphate 127-07-1, Hydroxyurea 143-67-9, Vinblastine sulfate 148-82-3, Melphalan 151-73-5, Betamethasone sodium phosphate 154-93-8, Carmustine 302-79-4, Tretinoin 305-03-3 366-70-1, Procarbazine hydrochloride 378-44-9, Betamethasone 595-33-5, Megestrol acetate 611-53-0, 5-Iodo-2'-deoxycytidine 645-05-6, Altretamine 968-93-4, Testolactone 1177-87-3, Dexamethasone acetate 1404-00-8, Mitomycin 1972-08-3, Dronabinol 2068-78-2, Vincalutoblastine, 22-oxo, sulfate (1:1) (salt) 2375-03-3, Methylprednisolone sodium succinate 3375-50-6 3778-73-2, Ifosfamide 4342-03-4, Dacarbazine 6000-74-4, Hydrocortisone sodium phosphate 7414-83-7, Etidronate disodium 9015-68-3, Asparaginase 9041-93-4, Bleomycin sulfate 11096-26-7, Erythropoietin 13010-47-4, Lomustine 13311-84-7, Flutamide 15663-27-1, Cisplatin 16595-80-5, Levamisole hydrochloride 17795-21-0, Allopurinol sodium salt 18378-89-7, Plitacemycin 18883-66-4, Streptozocin 20537-88-6, Amifostine 23541-50-6, Daunorubicin hydrochloride 24584-09-6, Dexrazoxane 25316-40-9, Doxorubicin hydrochloride 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 52205-73-9, Estramustine phosphate sodium 53910-25-1,

Pentostatin 54965-24-1, Tamoxifen citrate 56124-62-0, Valrubicin 57248-88-1, Pamidronate disodium 57852-57-0, Idarubicin hydrochloride 63612-50-0, Nilutamide 65271-80-9, Mitoxantrone 69304-47-8, BVDU 74381-53-6, Leuprolide acetate 77181-69-2, (E)-5-(2-Bromovinyl)-1- β -D-arabinofuranosyluracil 79517-01-4, Octreotide acetate 86386-73-4, Fluconazole 89778-27-8, Toremifene citrate 90357-06-5, Bicalutamide 90409-78-2, Polifeprosan 99614-01-4, Ondansetron hydrochloride 100286-90-6, Irinotecan hydrochloride 107007-99-8, Granisetron hydrochloride 110942-02-4, Aldesleukin 114977-28-5, Docetaxel 115956-13-3, Dolasetron mesylate 117091-64-2, Etoposide phosphate 119413-54-6, Topotecan hydrochloride 120511-73-1, Anastrozole 121181-53-1, Filgrastim 122111-03-9, Gemcitabine hydrochloride 123774-72-1, Sargramostim 125317-39-7, Vinorelbine tartrate 130167-69-0, Pegaspargase 145781-92-6, Goserelin acetate 173146-27-5, Denileukin diftitox 174722-31-7, Rituximab 180288-69-1, Trastuzumab 371770-68-2 554399-09-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(substituted nucleosides for prevention of drug resistance in cytostatic treatment)

IT 33069-62-4, Paclitaxel 74381-53-6, Leuprolide acetate 114977-28-5, Docetaxel 145781-92-6, Goserelin acetate

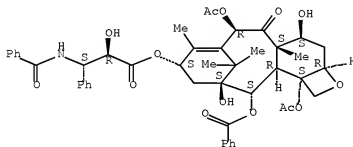
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(substituted nucleosides for prevention of drug resistance in cytostatic treatment)

RN 33069-62-4 CAPLUS

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (aR,BS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 74381-53-6 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)-, acetate (1:1) (CA INDEX NAME)

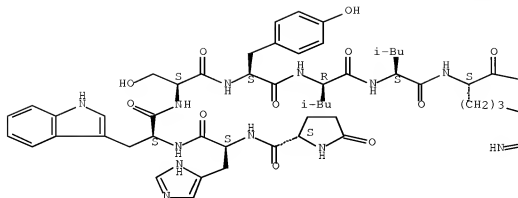
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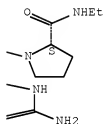
CMF C59 H84 N16 O12

Absolute stereochemistry. Rotation (-).

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CM 2

CRN 64-19-7

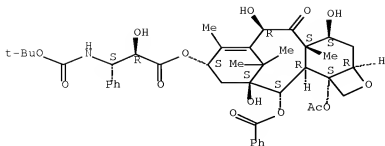
CMF C2 H4 O2



RN 114977-28-5 CAPLUS

CN Benzenepropanoic acid, β-[[[(1,1-dimethylethoxy)carbonyl]amino]-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 145781-92-6 CAPLUS

CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide, acetate (1:?) (CA INDEX NAME)

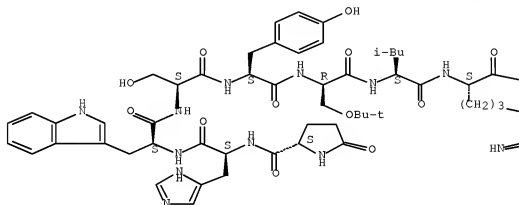
CM 1

CRN 65807-02-5

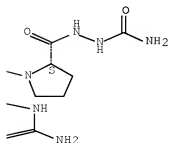
CMF C59 H84 N18 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2

REFERENCE COUNT: 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 11 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:376891 CAPLUS Full-text
 DOCUMENT NUMBER: 138:390865
 TITLE: Conjugate for treating by boron neutron capture (BNC) radiation-resistant tumors
 INVENTOR(S): Braun, Klaus; Waldeck, Waldemar; Pipkorn, Ruediger; Braun, Isabell; Debus, Juergen; Wolber, Gerd; Ehemann, Volker
 PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung Des Oeffentlichen Rechts, Germany
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040175	A1	20030515	WO 2002-DE4155	20021108 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10154830	A1	20030612	DE 2001-10154830	20011108 <--
AU 2002347109	A1	20030519	AU 2002-347109	20021108 <--
PRIORITY APPLN. INFO.:			DE 2001-10154830	A 20011108 <--
			WO 2002-DE4155	W 20021108

AB The invention concerns conjugates comprising the following individual elements: (a) a transport mediator for the cell membrane; (b) an addressing protein or peptide for import into the cell nucleus; and (c) the boron-10 derivative to be transported. The invention also concerns the use of said conjugates for treating glioblastoma by boron neutron capture therapy (BNCT). Preferably, a cleavable covalent disulfide bond links (a) and (b). Thus [D,L-boronophenylalanine]10 was conjugated to a nuclear localization sequence from SV40-T-antigen as address peptide; the address peptide's other end was linked to a human transport peptide unit. For electron microscopic purposes a glycine-lysine-conjugated FITC was added to the conjugate.

IC ICM C07K007-06
 ICS C07K014-025; C12N015-11; C12N015-62; A61K041-00; A61K038-17;
 A61K047-48

CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 8

IT Neuroglia, neoplasms
 (glioblastoma; conjugate for treating by boron neutron capture (BNC)
 radiation-resistant tumors)

IT 524943-98-4
 RL: BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant);
 BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (amino acid sequence, nuclear localization sequence from
 SV40-T-antigen; conjugate for treating by boron neutron capture (BNC)
 radiation-resistant tumors)

IT 95088-49-6D, conjugate with [D,L-boronophenylalanine]10
 108045-03-0D, conjugate with [D,L-boronophenylalanine]10
 524943-99-5
 RL: BUU (Biological use, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amino acid sequence; conjugate for treating by boron neutron capture
 (BNC) radiation-resistant tumors)

IT 524944-91-0DP, conjugate with transport peptide
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (for BNCT; conjugate for treating by boron neutron capture (BNC)
 radiation-resistant tumors)

IT 524944-92-1DP, FITC labeled, conjugate with transport peptide
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU
 (Therapeutic use); ANST (Analytical study); BIOL (Biological study);
 PREP (Preparation); USES (Uses)
 (for confocal laser-scanning microscopy; conjugate for treating by
 boron neutron capture (BNC) radiation-resistant tumors)

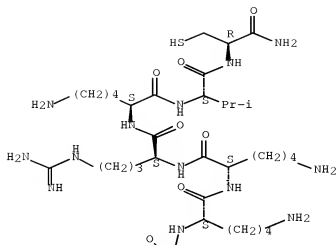
IT 524943-98-4
 RL: BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant);
 BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (amino acid sequence, nuclear localization sequence from
 SV40-T-antigen; conjugate for treating by boron neutron capture (BNC)
 radiation-resistant tumors)

RN 524943-98-4 CAPLUS

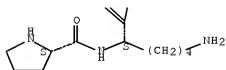
CN L-Cysteinamide, L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-lysyl-L-valyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

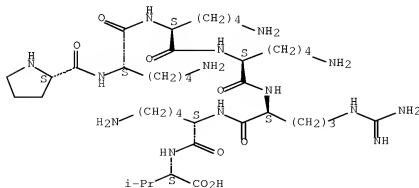


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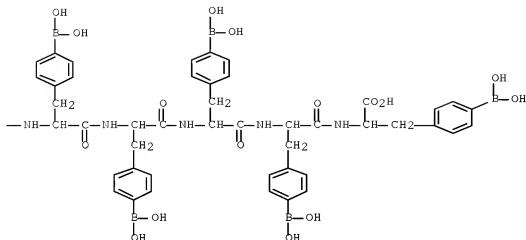


IT 95088-49-6D, conjugate with [D,L-boronophenylalanine]10
 108045-03-0D, conjugate with [D,L-boronophenylalanine]10
 524943-99-5
 RL: BUU (Biological use, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amino acid sequence; conjugate for treating by boron neutron capture
 (BNC) radiation-resistant tumors)
 RN 95088-49-6 CAPLUS
 CN L-Valine, L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-lysyl- (CA INDEX
 NAME)

Absolute stereochemistry.

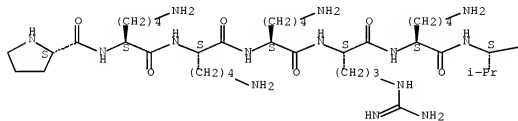


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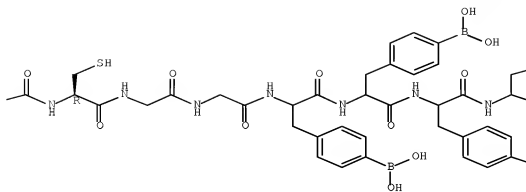
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Absolute stereochemistry.

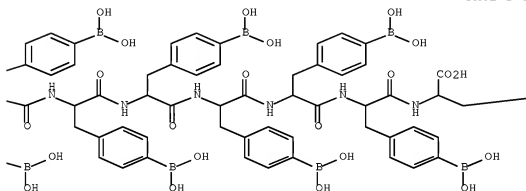
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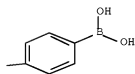
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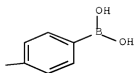


PAGE 1-D



IT 524944-92-1DP, FITC labeled, conjugate with transport peptide
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU
 (Therapeutic use); ANST (Analytical study); BIOL (Biological study);
 PREP (Preparation); USES (Uses)
 (for confocal laser-scanning microscopy; conjugate for treating by
 boron neutron capture (BNC) radiation-resistant tumors)
 RN 524944-92-1 CAPLUS
 CN Phenylalanine, L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-lysyl-L-valyl-
 L-cysteinylglycyl-L-lysyl-4-boronophenylalanyl-4-boronophenylalanyl-4-

PAGE 1-D



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 12 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:319448 CAPLUS Full-text
 DOCUMENT NUMBER: 138:331672
 TITLE: Compounds and methods for modulating cell adhesion-mediated drug resistance
 INVENTOR(S): Dalton, William S.; Damiano, Jason S.; Cress, Anne E.
 PATENT ASSIGNEE(S): University of South Florida, USA
 SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont. Ser. No. US 2001-795484, filed on 1 Mar 2001
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030078210	A1	20030424	US 2001-24017	20011221 <--
US 6812003	B2	20041102		
US 20050113305	A1	20050526	US 2004-978202	20041029 <--
US 7253149	B2	20070807		
US 20080051346	A1	20080228	US 2007-731947	20070330 <--
PRIORITY APPLN. INFO.:			US 2001-795484	A1 20010301 <--
			US 2000-186198P	P 20000301 <--
			US 2001-24017	A1 20011221 <--
			US 2004-978202	A1 20041029

AB Peptides and methods of their use for inhibiting drug and radiation-therapy resistance in cancerous cells in which efficacy of chemotherapy and/or radiotherapy of a patient is enhanced by administration of an effective amount of a peptide that inhibits cell adhesion-mediated drug resistance (CAM-DR). Preferably, the peptide comprises D-amino acids having the sequence: kmviywkag (RZ-3) or is a variant or modified version thereof. The peptide is preferably administered to the patient prior to chemotherapy and/or radiation therapy. Inhibition of CAM-DR by RZ-3 in multiple myeloma cells is disclosed.

IC ICM A61K038-10
 ICS A61K038-08
 INCL 514015000; 514016000
 CC 1-6 (Pharmacology)
 IT Antitumor agents
 Human

(peptides modulating cell adhesion-mediated drug resistance)

IT Antitumor agents
(resistance to, cell adhesion-mediated; peptides modulating cell
adhesion-mediated drug resistance)

IT Multiple myeloma
Neoplasm
(treatment of; peptides modulating cell adhesion-mediated drug
resistance)

IT 514181-06-7
RL: BSU (Biological study, unclassified); PAC (Pharmacological
activity); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(peptides modulating cell adhesion-mediated drug resistance)

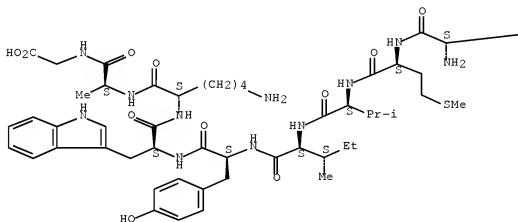
IT 514181-06-7
RL: BSU (Biological study, unclassified); PAC (Pharmacological
activity); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(peptides modulating cell adhesion-mediated drug resistance)

RN 514181-06-7 CAPLUS

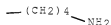
CN Glycine, L-lysyl-L-methionyl-L-valyl-L-isoleucyl-L-tyrosyl-L-tryptophyl-L-
L-tyrosyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 13 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:133050 CAPLUS Full-text
DOCUMENT NUMBER: 138:163521
TITLE: Improved treatment of cancer with irinotecan based on

INVENTOR(S): genotyping of human genes
 Heinrich, Guenther; Kerb, Reinhold
 PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany
 SOURCE: PCT Int. Appl., 130 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013537	A2	20030220	WO 2002-EP8218	20020723 <--
WO 2003013537	A3	20030925		
WO 2003013537	A9	20040429		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2454648	A1	20030220	CA 2002-2454648	20020723 <--
AU 2002328952	A1	20030224	AU 2002-328952	20020723 <--
EP 1438050	A2	20040721	EP 2002-764763	20020723 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005501840	T	20050120	JP 2003-518546	20020723 <--
PRIORITY APPLN. INFO.:			EP 2001-117608	A 20010723 <--
			EP 2002-11710	A 20020524 <--
			WO 2002-EP8218	W 20020723 <--
AB	The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with variant alleles of multidrug resistance genes MDR1 and MRP1, cytochrome P 450 gene CYP3A5, and UDP glycosyltransferase 1 gene UGT1A1. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.			
IC	ICM A61K031-4745 ICS A61P035-00			
CC	1-6 (Pharmacology)			
IT	Section cross-reference(s): 3 Uterus, neoplasm (cervix; improved treatment of cancer with irinotecan based on genotyping of human genes)			
IT	Intestine, neoplasm (colorectal; improved treatment of cancer with irinotecan based on genotyping of human genes)			
IT	Animals Antitumor agents			

Drug resistance
 Genotyping (method)
 Human
 Lung, neoplasm
 Mus
 Neuroglia, neoplasm
 Ovary, neoplasm
 Pancreas, neoplasm
 Stomach, neoplasm
 (improved treatment of cancer with irinotecan based on genotyping of human genes)

IT 496954-10-0 496954-11-1 497271-30-4 497271-31-5
 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA topoisomerase I allele fragment; improved treatment of cancer with
 irinotecan based on genotyping of human genes)

IT 496953-51-6 496953-52-7 496953-53-8
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 497271-07-5 497271-08-6 497271-09-7 497271-10-0 497271-11-1
 497271-12-2 497271-13-3
 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (UDP glucosyltransferase 1 allele fragment; improved treatment of
 cancer with irinotecan based on genotyping of human genes)

IT 496953-86-7 496953-88-9 496953-90-3
 496953-92-5 496953-94-7 496953-95-8
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 497271-22-4 497271-23-5 497271-24-6 497271-25-7 497271-26-8
 497271-27-9 497271-28-0 497271-29-1
 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (multidrug resistance protein MRP1 allele fragment; improved
 treatment of cancer with irinotecan based on genotyping of human genes)

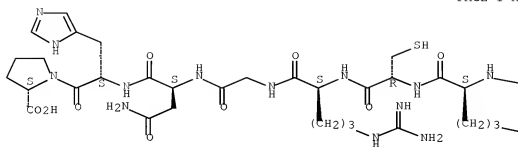
IT 496954-10-0 496954-11-1
 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA topoisomerase I allele fragment; improved treatment of cancer with
 irinotecan based on genotyping of human genes)

RN 496954-10-0 CAPLUS

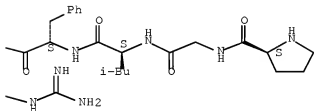
CN L-Proline, L-prolylglycyl-L-leucyl-L-phenylalanyl-L-arginyl-L-cysteinyl-L-
 arginylglycyl-L-asparaginyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

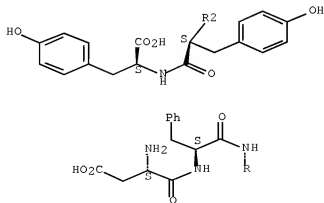


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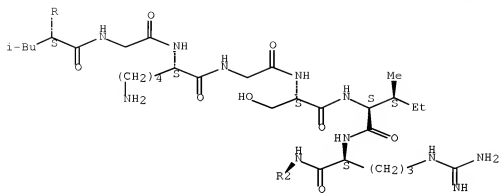
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Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 496953-51-6 496953-52-7 496953-53-8
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RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)

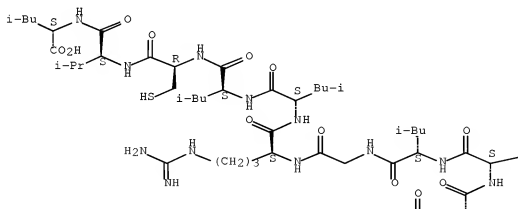
(UDP glucosyltransferase 1 allele fragment; improved treatment of
 cancer with irinotecan based on genotyping of human genes)

RN 496953-51-6 CAPLUS

CN L-Leucine, L-prolyl-L-leucyl-L-valyl-L-leucylglycyl-L-arginyl-L-leucyl-L-
 leucyl-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)

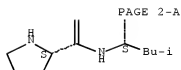
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

Pr-i

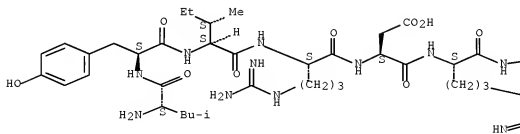


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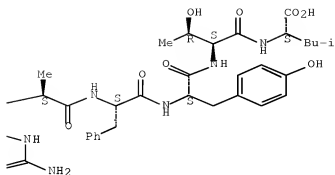
CN L-Leucine, L-leucyl-L-tyrosyl-L-isoleucyl-L-arginyl-L- α -aspartyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

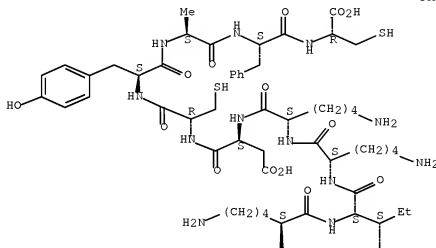


RN 496953-53-8 CAPLUS

CN L-Cysteine, L-lysyl-L-lysyl-L-isoleucyl-L-lysyl-L-lysyl-L- α -aspartyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

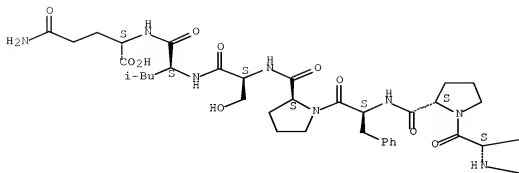


RN 496953-54-9 CAPLUS

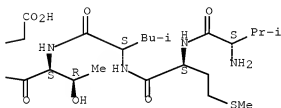
CN L-Glutamine, L-valyl-L-methionyl-L-leucyl-L-threonyl-L- α -aspartyl-L-prolyl-L-phenylalanyl-L-prolyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

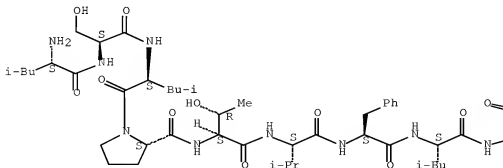


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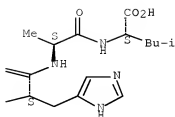
CN L-Leucine, L-leucyl-L-seryl-L-leucyl-L-prolyl-L-threonyl-L-valyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

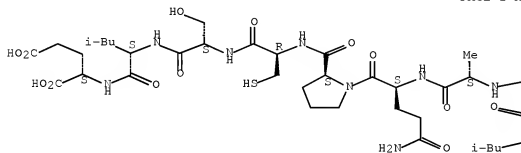


RN 496953-56-1 CAPLUS

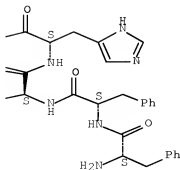
CN L-Glutamic acid, L-phenylalanyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl-L-glutamyl-L-prolyl-L-cysteinyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

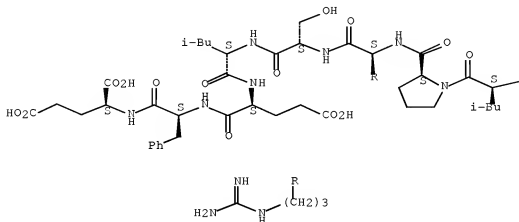


RN 496953-57-2 CAPLUS

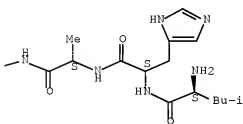
CN L-Glutamic acid, L-leucyl-L-histidyl-L-alanyl-L-leucyl-L-prolyl-L-arginyl-L-seryl-L-leucyl-L- α -glutamyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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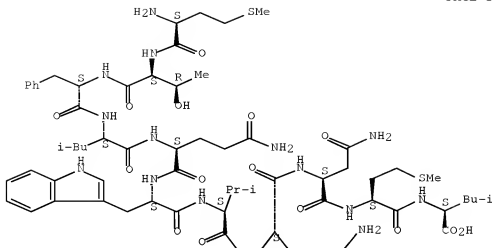


RN 496953-58-3 CAPLUS

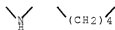
CN L-Leucine, L-methionyl-L-threonine, L-phenylalanyl-L-leucyl-L-glutamyl-L-tryptophyl-L-valyl-L-lysyl-L-asparaginyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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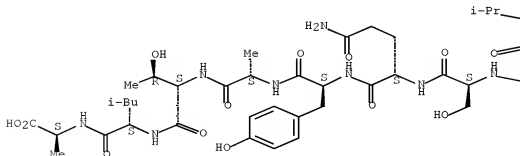


RN 496953-59-4 CAPLUS

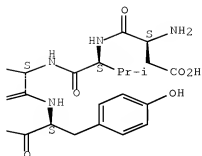
CN L-Alanine, L- α -aspartyl-L-valyl-L-valyl-L-tyrosyl-L-seryl-L-glutaminy-L-tyrosyl-L-alanyl-L-threonyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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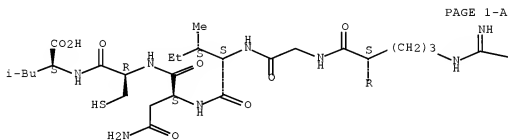
PAGE 1-B



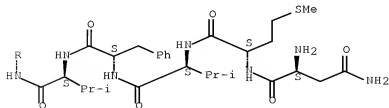
RN 496953-60-7 CAPLUS

CN L-Leucine, L-asparaginyl-L-methionyl-L-valyl-L-phenylalanyl-L-valyl-L-
arginylglycyl-L-isoleucyl-L-asparaginyl-L-cysteinyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



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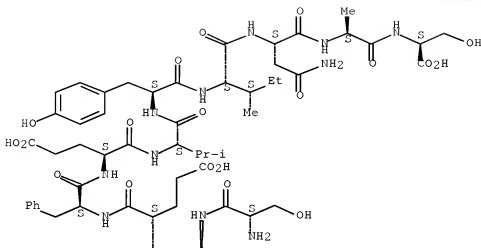
RN 496953-61-8 CAPLUS

CN L-Serine, L-seryl-L-glutamyl-L- α -glutamyl-L-phenylalanyl-L- α -glutamyl-L-valyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-alanyl- (9CI) (CA

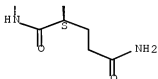
INDEX NAME)

Absolute stereochemistry.

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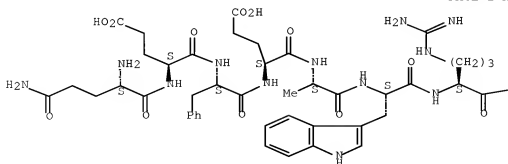


RN 496953-63-0 CAPLUS

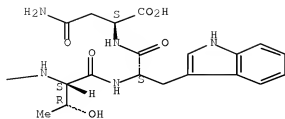
CN L-Asparagine, L-glutaminyl-L- α -glutamyl-L-phenylalanyl-L- α -glutamyl-L-alanyl-L-tryptophyl-L-arginyl-L-threonyl-L-tryptophyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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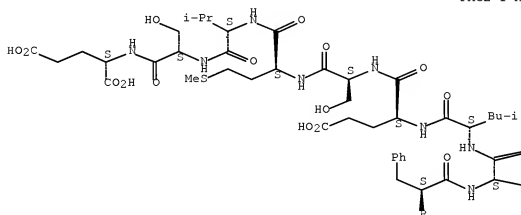


RN 496953-64-1 CAPLUS

CN L-Glutamic acid, L-valyl-L-valyl-L-phenylalanyl-L-seryl-L-leucyl-L- α -glutamyl-L-seryl-L-methionyl-L-valyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

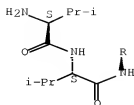
PAGE 1-A



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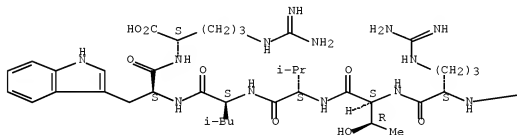


RN 496953-65-2 CAPLUS

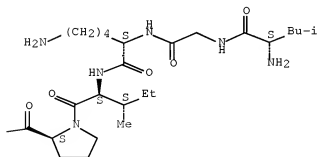
CN L-Arginine, L-leucylglycyl-L-lysyl-L-isoleucyl-L-prolyl-L-arginyl-L-threonyl-L-valyl-L-leucyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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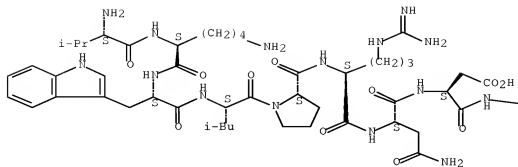


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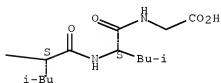
CN Glycine, L-valyl-L-lysyl-L-tryptophyl-L-leucyl-L-prolyl-L-arginyl-L-asparaginyl-L-α-aspartyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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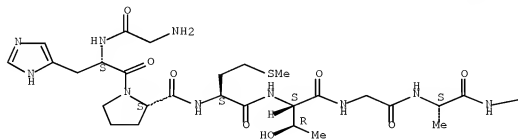


RN 496953-67-4 CAPLUS

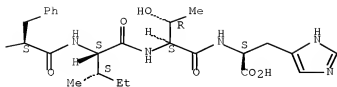
CN L-Histidine, glycyl-L-histidyl-L-prolyl-L-methionyl-L-threonylglycyl-L-alanyl-L-phenylalanyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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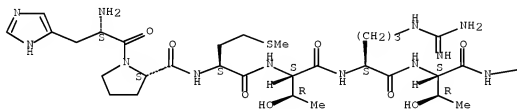


RN 496953-68-5 CAPLUS

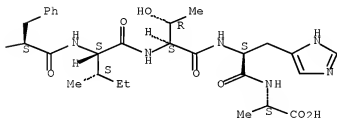
CN L-Alanine, L-histidyl-L-prolyl-L-methionyl-L-threonyl-L-arginyl-L-threonyl-L-phenylalanyl-L-isoleucyl-L-threonyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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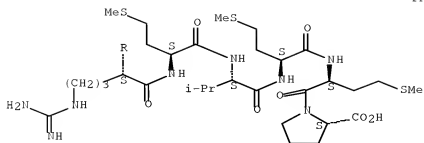


RN 496953-69-6 CAPLUS

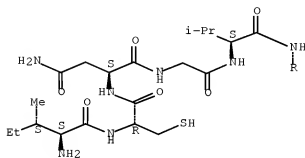
CN L-Proline, L-isoleucyl-L-cysteinyl-L-asparaginylglycyl-L-valyl-L-arginyl-L-methionyl-L-valyl-L-methionyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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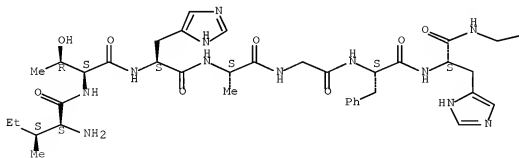


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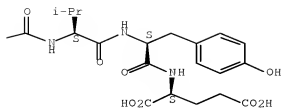
CN L-Glutamic acid, L-isoleucyl-L-threonyl-L-histidyl-L-alanylglycyl-L-phenylalanyl-L-histidylglycyl-L-valyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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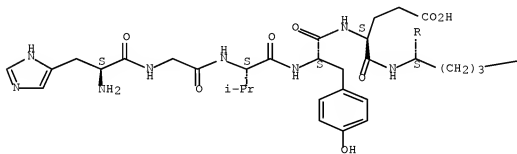


RN 496953-71-0 CAPLUS

CN L-Valine, L-histidylglycyl-L-valyl-L-tyrosyl-L- α -glutamyl-L-arginyl-L-isoleucyl-L-cysteinyl-L-asparaginylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

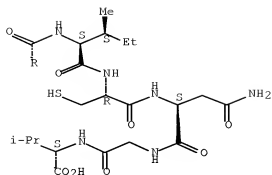
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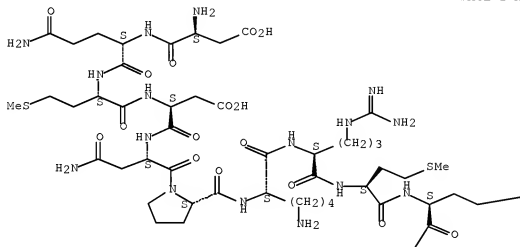


RN 496953-72-1 CAPLUS

CN L-Threonine, L- α -aspartyl-L-glutaminyl-L-methionyl-L- α -
 aspartyl-L-asparaginyl-L-prolyl-L-lysyl-L-arginyl-L-methionyl-L- α -
 glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

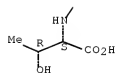
PAGE 1-A



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—CO₂H

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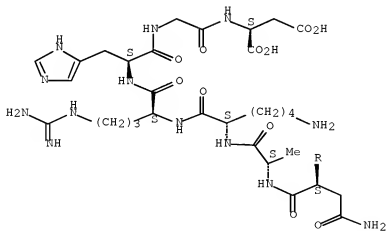


RN 496953-73-2 CAPLUS

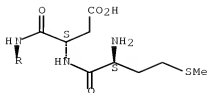
CN L-Aspartic acid, L-methionyl-L- α -aspartyl-L-asparaginyl-L-alanyl-L-lysyl-L-arginyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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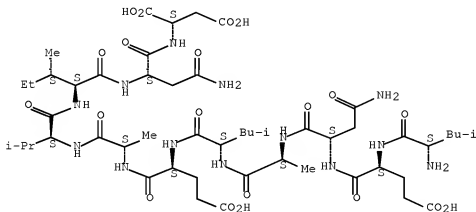
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RN 496953-74-3 CAPLUS

CN L-Aspartic acid, L-leucyl-L- α -glutamyl-L-asparaginyl-L-alanyl-L-leucyl-L- α -glutamyl-L-alanyl-L-valyl-L-isoleucyl-L-asparaginyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

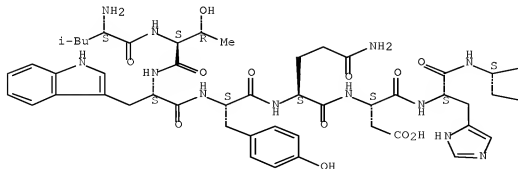


RN 496953-75-4 CAPLUS

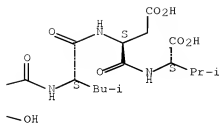
CN L-Valine, L-leucyl-L-threonyl-L-tryptophyl-L-tyrosyl-L-glutaminyl-L- α -aspartyl-L-histidyl-L-seryl-L-leucyl-L- α -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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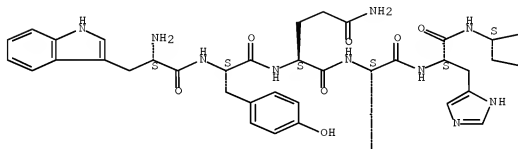


RN 496953-76-5 CAPLUS

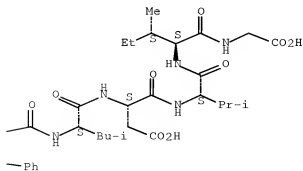
CN Glycine, L-tryptophyl-L-tyrosyl-L-glutaminyl-L-tyrosyl-L-histidyl-L-phenylalanyl-L-leucyl-L- α -aspartyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

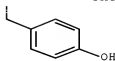
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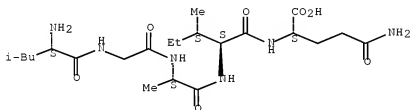
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RN 496953-77-6 CAPLUS

CN L-Glutamine, L-leucylglycyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

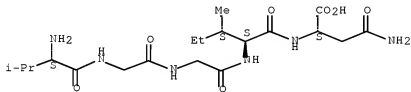
Absolute stereochemistry.



RN 496953-78-7 CAPLUS

CN L-Asparagine, L-valylglycylglycyl-L-isoleucyl- (9CI) (CA INDEX NAME)

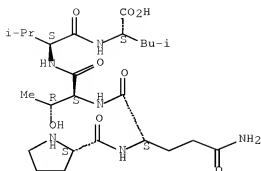
Absolute stereochemistry.



RN 496953-80-1 CAPLUS

CN L-Leucine, L-prolyl-L-glutamyl-L-threonyl-L-valyl- (9CI) (CA INDEX NAME)

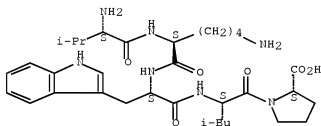
Absolute stereochemistry.



RN 496953-81-2 CAPLUS

CN L-Proline, L-valyl-L-lysyl-L-tryptophyl-L-leucyl- (9CI) (CA INDEX NAME)

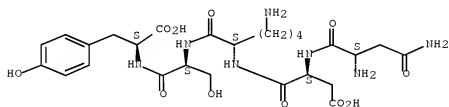
Absolute stereochemistry.



RN 496953-83-4 CAPLUS

CN L-Tyrosine, L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 496953-96-7 496953-88-3 496953-90-3

496953-92-5 496953-94-7 496953-95-3

496953-97-0 496953-98-1 496953-99-2

496954-00-8 496954-01-9 496954-02-0

496954-04-2 496954-05-3 496954-07-5

496954-09-7

RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human genes)

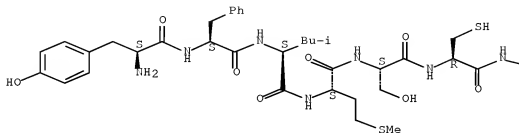
RN 496953-86-7 CAPLUS

CN L-Isoleucine, L-tyrosyl-L-phenylalanyl-L-leucyl-L-methionyl-L-seryl-L-

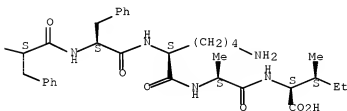
cysteiny-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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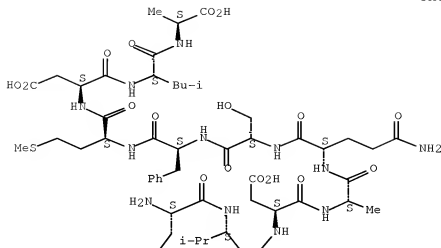


RN 496953-88-9 CAPLUS

CN L-Alanine, L-seryl-L-valyl-L- α -aspartyl-L-alanyl-L-glutaminyl-L-seryl-L-phenylalanyl-L-methionyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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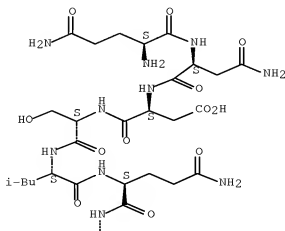


RN 496953-90-3 CAPLUS

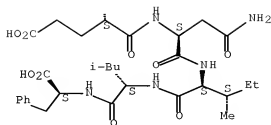
CN L-Phenylalanine, L-glutaminyl-L-asparaginyll-L- α -aspartyl-L-seryl-L-leucyl-L-glutaminyl-L- α -glutamyl-L-asparaginyll-L-isoleucyl-L-leucyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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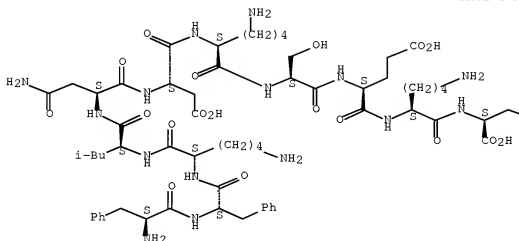


RN 496953-92-5 CAPLUS

CN L-Aspartic acid, L-phenylalanyl-L-phenylalanyl-L-lysyl-L-leucyl-L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl-L- α -glutamyl-L-lysyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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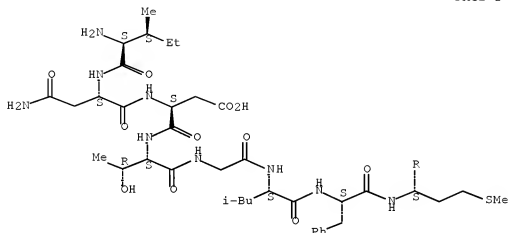
PAGE 1-B

RN 496953-94-7 CAPLUS

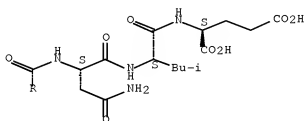
CN L-Glutamic acid, L-isoleucyl-L-asparaginyl-L- α -aspartyl-L-threonylglycyl-L-leucyl-L-phenylalanyl-L-methionyl-L-asparaginyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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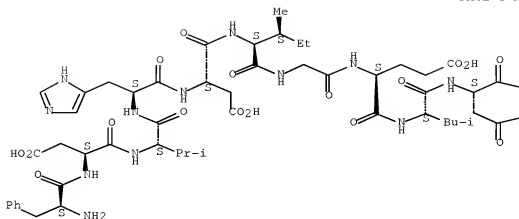


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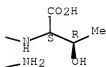
CN L-Threonine, L-phenylalanyl-L- α -aspartyl-L-valyl-L-histidyl-L- α -aspartyl-L-isoleucylglycyl-L- α -glutamyl-L-leucyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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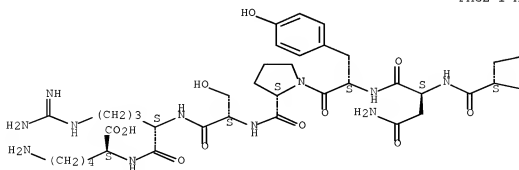


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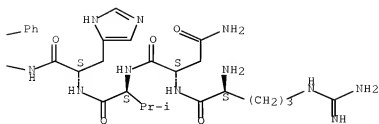
CN L-Lysine, L-arginyl-L-asparaginyl-L-valyl-L-histidyl-L-phenylalanyl-L-asparaginyl-L-tyrosyl-L-prolyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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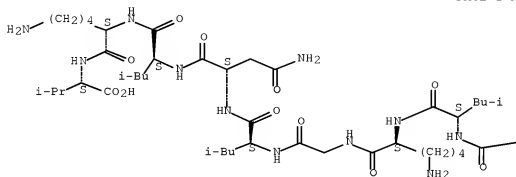


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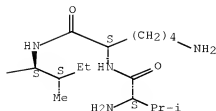
CN L-Valine, L-valyl-L-lysyl-L-isoleucyl-L-leucyl-L-lysylglycyl-L-leucyl-L-asparaginyll-L-leucyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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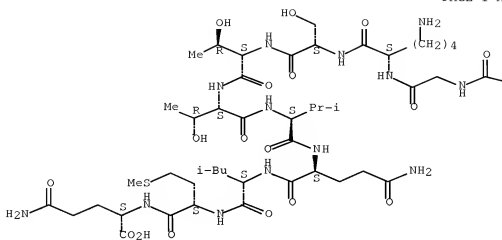


RN 496953-99-2 CAPLUS

CN L-Glutamine, L-cysteinyglycyl-L-lysyl-L-seryl-L-threonyl-L-threonyl-L-valyl-L-glutaminyll-L-leucyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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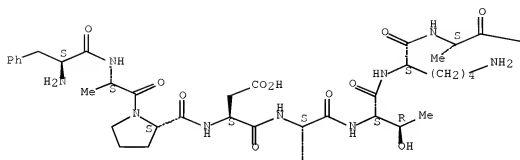


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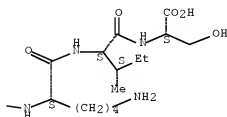
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Absolute stereochemistry.

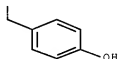
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PAGE 1-B



PAGE 2-A

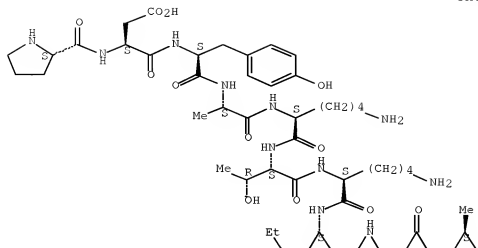


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Absolute stereochemistry.

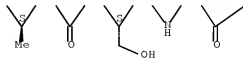
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PAGE 1-B



PAGE 2-A



PAGE 2-B

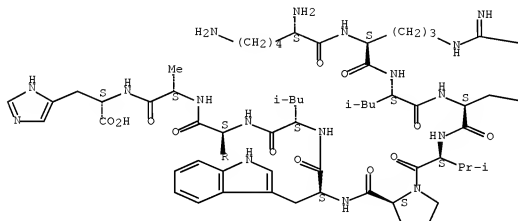


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Absolute stereochemistry.

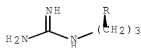
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PAGE 1-B



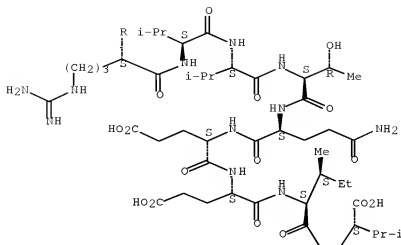
PAGE 2-A



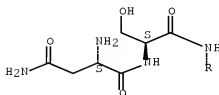
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PAGE 2-A

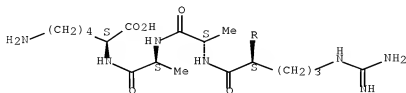


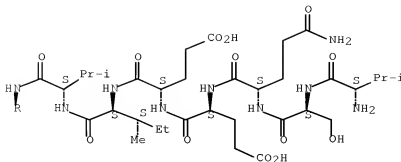
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Absolute stereochemistry.

PAGE 1-A





L80 ANSWER 14 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:133049 CAPLUS Full-text

DOCUMENT NUMBER: 138:163520

TITLE: Improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1

INVENTOR(S): Heinrich, Guenther; Kerb, Reinhold

PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013536	A2	20030220	WO 2002-EP8217	20020723 <--
WO 2003013536	A3	20031218		
WO 2003013536	A9	20040429		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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PRIORITY APPLN. INFO.:			EP 2001-117608	A 20010723 <--
			EP 2002-11710	A 20020524 <--
			WO 2002-EP8217	W 20020723 <--

AB The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with

variant alleles of genes involved in irinotecan metabolism, and in particular UDP glycosyltransferase 1 gene UGT1A1. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.

IC ICM A61K031-4745
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3
IT Uterus, neoplasm
(cervix; improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)
IT Intestine, neoplasm
(colorectal; improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)
IT Animals
Antitumor agents
Drug resistance
Genotyping (method)
Human
Lung, neoplasm
Mus
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)
IT 496954-10-0 496954-11-1 497274-38-1 497274-39-2
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)
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497274-20-1 497274-21-2
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UDP glucosyltransferase 1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)

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 497274-35-8 497274-36-9 497274-37-0

RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (multidrug resistance protein MRP1 allele fragment; improved
 treatment of cancer with irinotecan based on genotyping of human gene
 UGT1A1 encoding UDP glycosyltransferase 1)

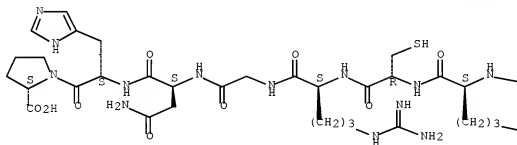
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 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA topoisomerase I allele fragment; improved treatment of cancer with
 irinotecan based on genotyping of human gene UGT1A1 encoding UDP
 glycosyltransferase 1)

RN 496954-10-0 CAPLUS

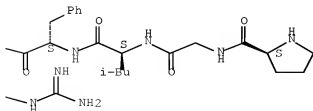
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Absolute stereochemistry.

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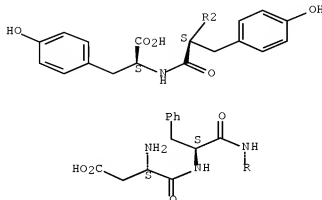


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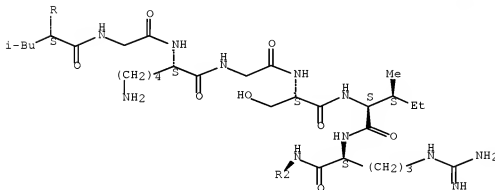
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Absolute stereochemistry.

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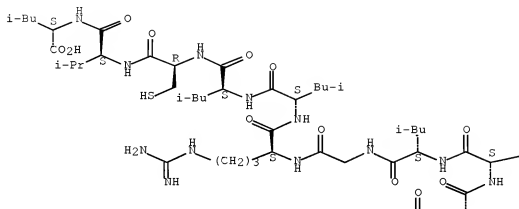


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 496953-76-5 496953-77-6 496953-78-7
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 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (UDP glucosyltransferase 1 allele fragment; improved treatment of
 cancer with irinotecan based on genotyping of human gene UGT1A1
 encoding UDP glucosyltransferase 1)
 RN 496953-51-6 CAPLUS
 CN L-Leucine, L-prolyl-L-leucyl-L-valyl-L-leucylglycyl-L-arginyl-L-leucyl-L-

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Absolute stereochemistry.

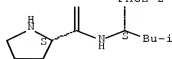
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Pr-i

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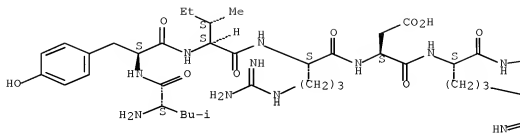


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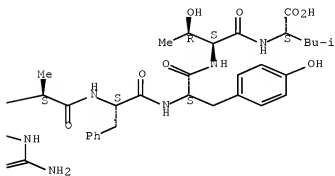
CN L-Leucine, L-leucyl-L-tyrosyl-L-isoleucyl-L-arginyl-L- α -aspartyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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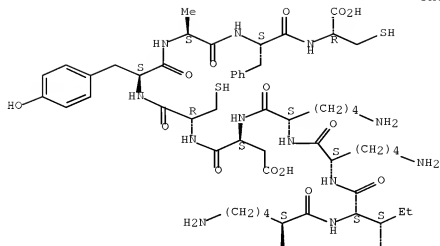


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Absolute stereochemistry.

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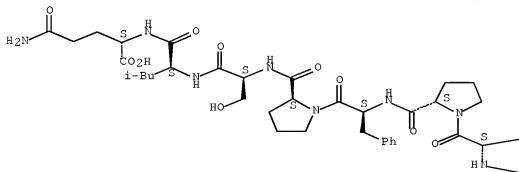


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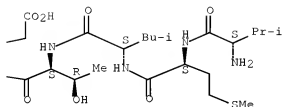
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Absolute stereochemistry.

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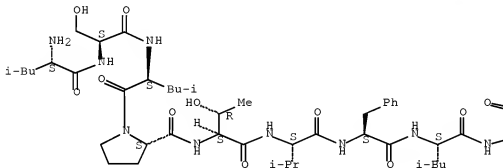


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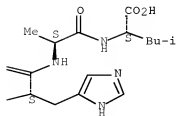
CN L-Leucine, L-leucyl-L-seryl-L-leucyl-L-prolyl-L-threonyl-L-valyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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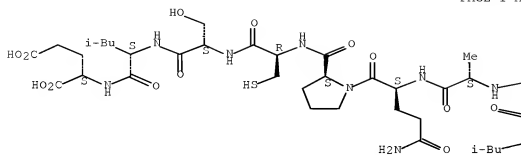
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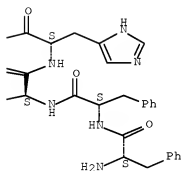
INDEX NAME)

Absolute stereochemistry.

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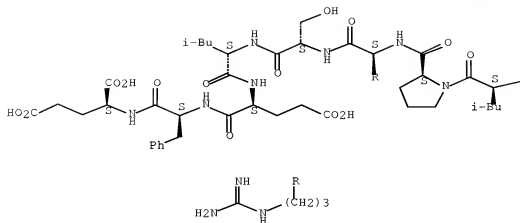


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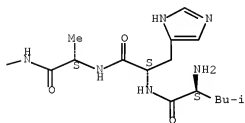
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Absolute stereochemistry.

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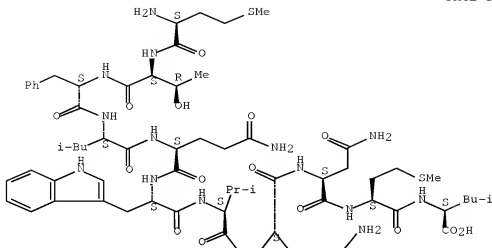


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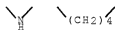
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Absolute stereochemistry.

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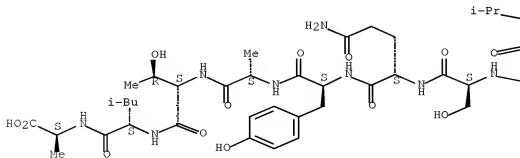


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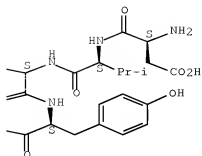
CN L-Alanine, L- α -aspartyl-L-valyl-L-valyl-L-tyrosyl-L-seryl-L-glutamyl-L-tyrosyl-L-alanyl-L-threonyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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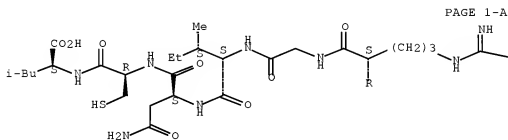
PAGE 1-B



RN 496953-60-7 CAPLUS

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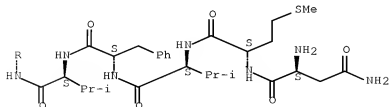
Absolute stereochemistry.



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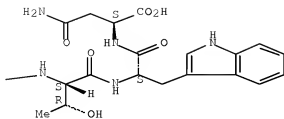
PAGE 2-A



RN 496953-61-8 CAPLUS

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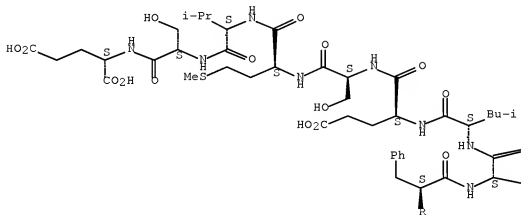


RN 496953-64-1 CAPLUS

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Absolute stereochemistry.

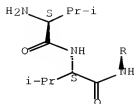
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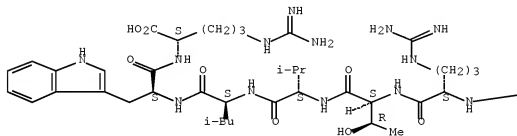


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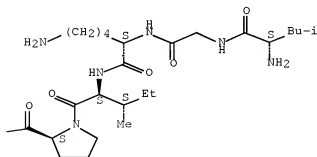
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Absolute stereochemistry.

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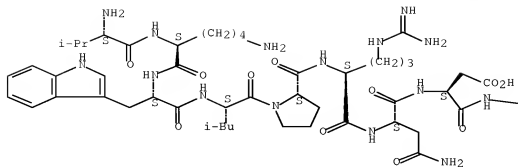


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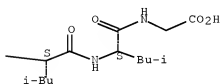
CN Glycine, L-valyl-L-lysyl-L-tryptophyl-L-leucyl-L-prolyl-L-arginyl-L-asparaginyl-L-α-aspartyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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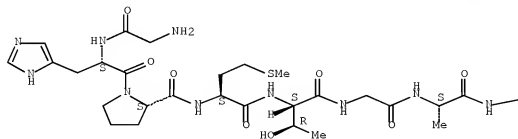


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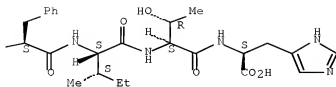
CN L-Histidine, glycyl-L-histidyl-L-prolyl-L-methionyl-L-threonylglycyl-L-alanyl-L-phenylalanyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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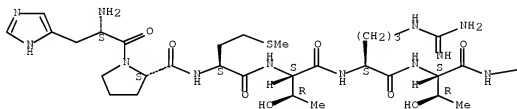


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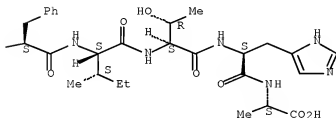
CN L-Alanine, L-histidyl-L-prolyl-L-methionyl-L-threonyl-L-arginyl-L-threonyl-L-phenylalanyl-L-isoleucyl-L-threonyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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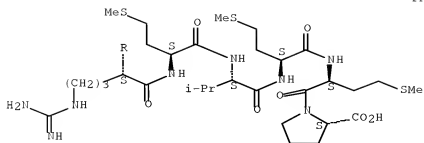


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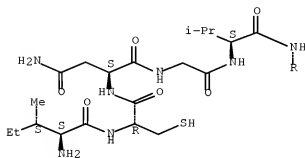
CN L-Proline, L-isoleucyl-L-cysteinyl-L-asparaginylglycyl-L-valyl-L-arginyl-L-methionyl-L-valyl-L-methionyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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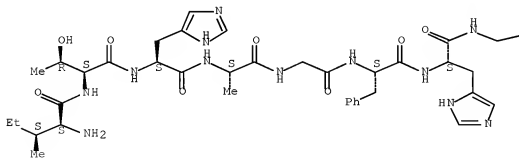


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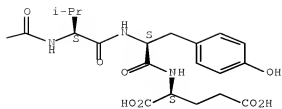
CN L-Glutamic acid, L-isoleucyl-L-threonyl-L-histidyl-L-alanylglycyl-L-phenylalanyl-L-histidylglycyl-L-valyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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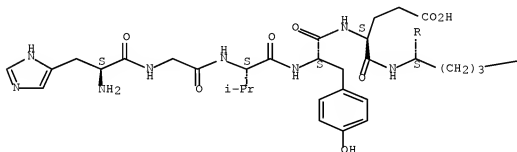


RN 496953-71-0 CAPLUS

CN L-Valine, L-histidylglycyl-L-valyl-L-tyrosyl-L- α -glutamyl-L-arginyl-L-isoleucyl-L-cysteinyl-L-asparaginyglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

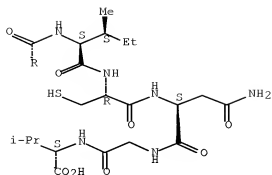
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PAGE 1-B



PAGE 2-A

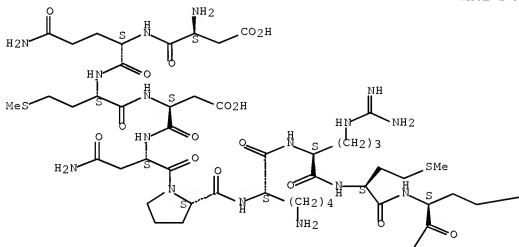


RN 496953-72-1 CAPLUS

CN L-Threonine, L- α -aspartyl-L-glutaminyl-L-methionyl-L- α -
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 glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

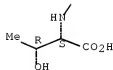
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—CO₂H

PAGE 2-A

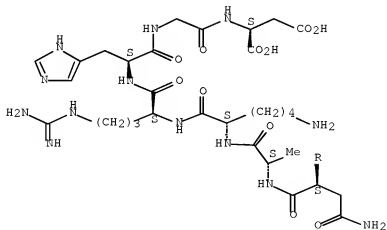


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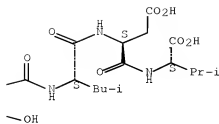
CN L-Aspartic acid, L-methionyl-L- α -aspartyl-L-asparaginyl-L-alanyl-L-lysyl-L-arginyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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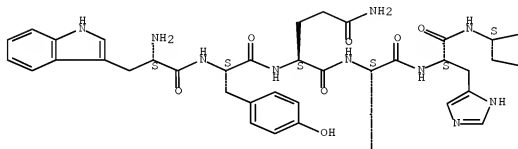


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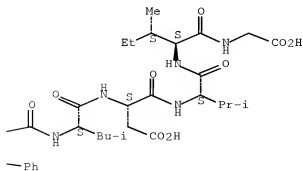
CN Glycine, L-tryptophyl-L-tyrosyl-L-glutaminyl-L-tyrosyl-L-histidyl-L-phenylalanyl-L-leucyl-L- α -aspartyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

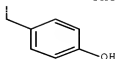
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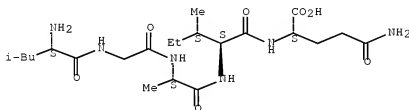
PAGE 2-A



RN 496953-77-6 CAPLUS

CN L-Glutamine, L-leucylglycyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

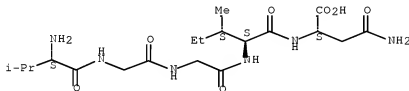
Absolute stereochemistry.



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CN L-Asparagine, L-valylglycylglycyl-L-isoleucyl- (9CI) (CA INDEX NAME)

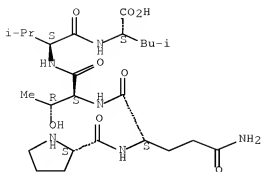
Absolute stereochemistry.



RN 496953-80-1 CAPLUS

CN L-Leucine, L-prolyl-L-glutamyl-L-threonyl-L-valyl- (9CI) (CA INDEX NAME)

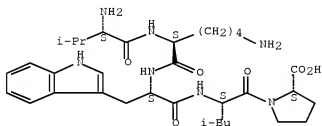
Absolute stereochemistry.



RN 496953-81-2 CAPLUS

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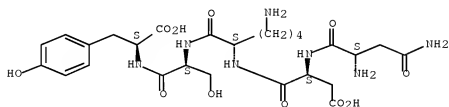
Absolute stereochemistry.



RN 496953-83-4 CAPLUS

CN L-Tyrosine, L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 496953-96-7 496953-88-3 496953-90-3

496953-92-5 496953-94-7 496953-95-3

496953-97-0 496953-98-1 496953-99-2

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496954-09-7

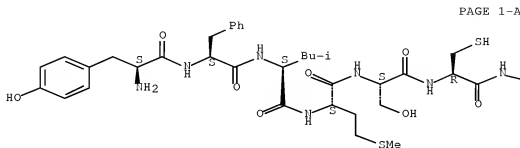
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene UGT1A1 encoding UDP glycosyltransferase 1)

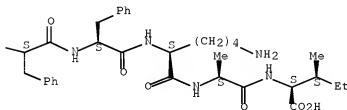
RN 496953-86-7 CAPLUS

CN L-Isoleucine, L-tyrosyl-L-phenylalanyl-L-leucyl-L-methionyl-L-seryl-L-cysteiny-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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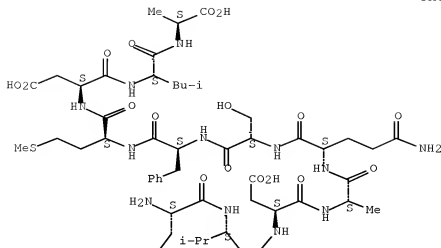


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CN L-Alanine, L-seryl-L-valyl-L- α -aspartyl-L-alanyl-L-glutaminy-L-seryl-L-phenylalanyl-L-methionyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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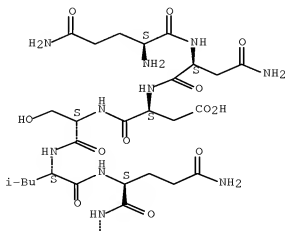


RN 496953-90-3 CAPLUS

CN L-Phenylalanine, L-glutaminyl-L-asparaginyl-L- α -aspartyl-L-seryl-L-leucyl-L-glutaminyl-L- α -glutamyl-L-asparaginyl-L-isoleucyl-L-leucyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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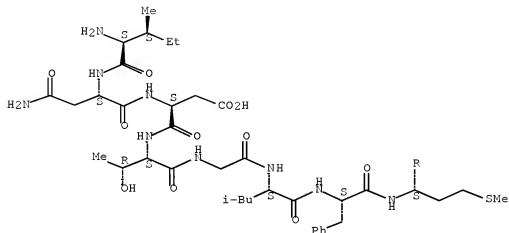


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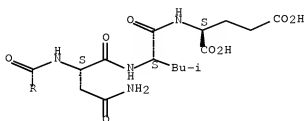
CN L-Glutamic acid, L-isoleucyl-L-asparaginyl-L- α -aspartyl-L-threonylglycyl-L-leucyl-L-phenylalanyl-L-methionyl-L-asparaginyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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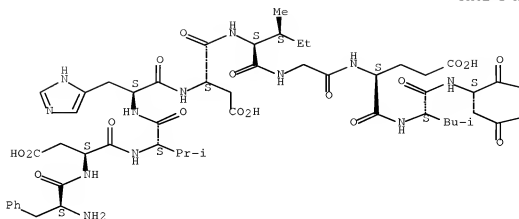


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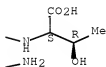
CN L-Threonine, L-phenylalanyl-L- α -aspartyl-L-valyl-L-histidyl-L- α -aspartyl-L-isoleucylglycyl-L- α -glutamyl-L-leucyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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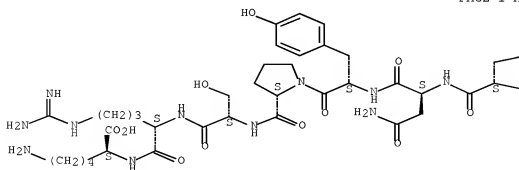


RN 496953-97-0 CAPLUS

CN L-Lysine, L-arginyl-L-asparaginyl-L-valyl-L-histidyl-L-phenylalanyl-L-asparaginyl-L-tyrosyl-L-prolyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

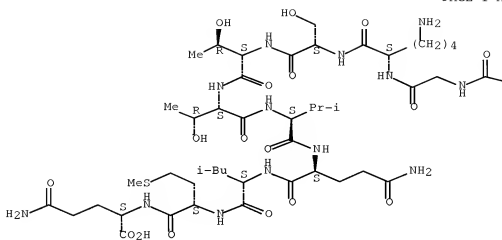
Absolute stereochemistry.

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Absolute stereochemistry.

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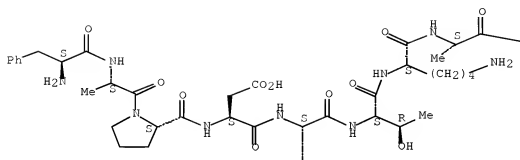


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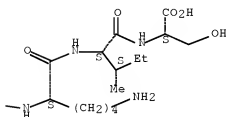
CN L-Threonine, L-lysyl-L- α -glutamyl-L-leucyl-L- α -glutamylglycyl-L-serylglycyl-L-lysyl-L-isoleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

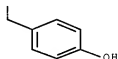
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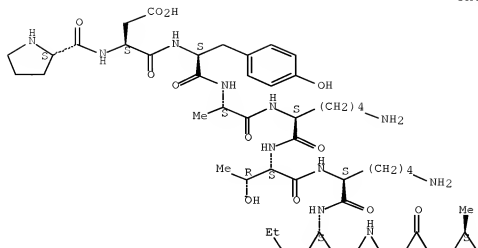


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CN L-Alanine, L-prolyl-L- α -aspartyl-L-tyrosyl-L-alanyl-L-lysyl-L-threonyl-L-lysyl-L-isoleucyl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

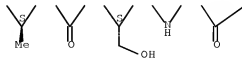
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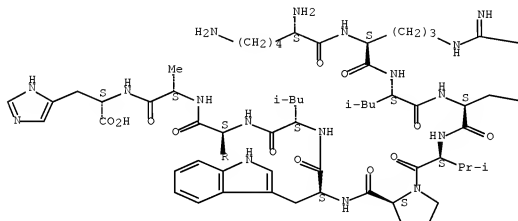


RN 496954-04-2 CAPLUS

CN L-Histidine, L-lysyl-L-arginyl-L-leucyl-L-asparaginyl-L-valyl-L-prolyl-L-tryptophyl-L-leucyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

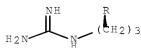
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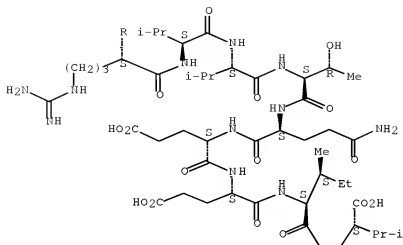
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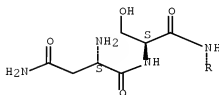
RN 496954-05-3 CAPLUS

CN L-Serine, L-isoleucyl-L-alanyl-L-α-glutamyl-L-asparaginyl-L-isoleucyl-L-alanyl-L-tyrosylglycyl-L-α-aspartyl-L-asparaginyl- (9CI)

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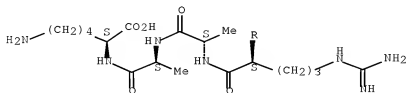


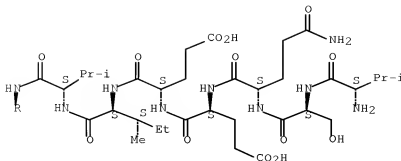
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CN L-Lysine, L-valyl-L-seryl-L-glutamyl-L- α -glutamyl-L- α -glutamyl-L-isoleucyl-L-valyl-L-arginyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L80 ANSWER 15 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:133048 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:163519

TITLE: Improved treatment of cancer with irinotecan based on

genotyping of human gene MDR1 encoding P-glycoprotein

INVENTOR(S): Heinrich, Guenther; Kerb, Reinhold

PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013535	A2	20030220	WO 2002-EP8220	20020723 <--
WO 2003013535	A3	20030925		
WO 2003013535	A9	20040429		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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PRIORITY APPLN. INFO.:			EP 2001-117608	A 20010723 <--
			EP 2002-11710	A 20020524 <--
			WO 2002-EP8220	W 20020723 <--

AB The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with variant alleles of genes involved in irinotecan metabolism, and in particular

the multidrug resistance gene MDR1. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.

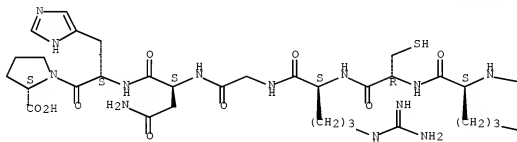
IC ICM A61K031-4741
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3
IT Uterus, neoplasm
(cervix; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)
IT Intestine, neoplasm
(colorectal; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)
IT Alleles
Animals
Antitumor agents
Drug resistance
Genotyping (method)
Human
Lung, neoplasm
Mus
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)
IT 496954-10-0 496954-11-1 497277-90-4 497277-91-5
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)
IT 496953-51-6 496953-52-7 496953-53-8
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497277-67-5 497277-68-6 497277-69-7 497277-70-0 497277-71-1
497277-72-2 497277-73-3
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UDP glucosyltransferase 1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)

IT	496953-66-7	496953-88-9	496953-90-3		
	496953-92-5	496953-94-7	496953-95-8		
	496953-97-0	496953-98-1	496953-99-2		
	496954-00-8	496954-01-9	496954-02-0		
	496954-04-2	496954-05-3	496954-07-5		
	496954-09-7	497277-74-4	497277-75-5	497277-76-6	
	497277-77-7	497277-78-8	497277-79-9	497277-80-2	497277-81-3
	497277-82-4	497277-83-5	497277-84-6	497277-85-7	497277-86-8
	497277-87-9	497277-88-0	497277-89-1		

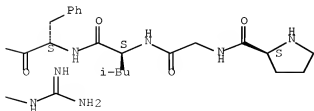
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)

IT	496954-10-0 496954-11-1 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)
RN	496954-10-0 CAPLUS
CN	L-Proline, L-polyglycyl-L-leucyl-L-phenylalanyl-L-arginyl-L-cysteinyl-L- arginylglycyl-L-asparaginyl-L-histidyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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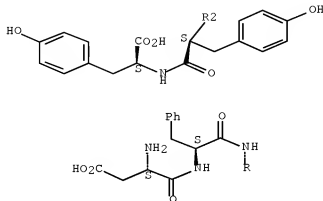
PAGE 1-B

RN 496954-11-1 CAPLUS

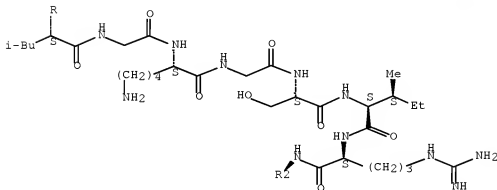
CN L-Tyrosine, L- α -aspartyl-L-phenylalanyl-L-leucylglycyl-L-lysylglycyl-L-seryl-L-isoleucyl-L-arginyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT	496953-51-6	496953-52-7	496953-53-8
	496953-54-9	496953-55-0	496953-56-1
	496953-57-2	496953-58-3	496953-59-1
	496953-60-7	496953-61-8	496953-62-0
	496953-64-1	496953-65-2	496953-66-3
	496953-67-4	496953-68-5	496953-69-6
	496953-70-9	496953-71-0	496953-72-1
	496953-73-2	496953-74-3	496953-75-4
	496953-76-5	496953-77-6	496953-78-7
	496953-80-1	496953-81-2	496953-83-4

RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(UDP glucosyltransferase 1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)

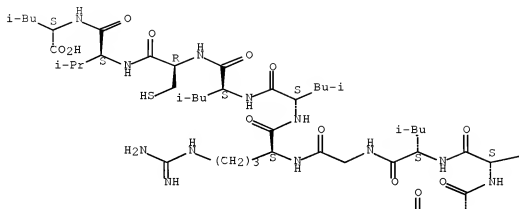
RN 496953-51-6 CAPLUS

CN L-Leucine, L-prolyl-L-leucyl-L-valyl-L-leucylglycyl-L-arginyl-L-leucyl-L-

leucyl-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

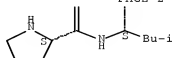
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Pr-i

PAGE 2-A

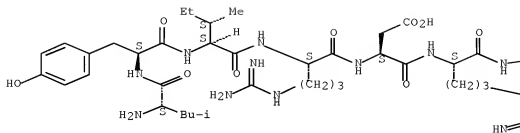


RN 496953-52-7 CAPLUS

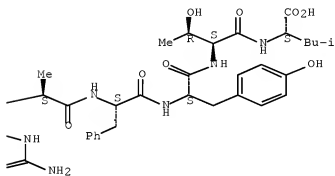
CN L-Leucine, L-leucyl-L-tyrosyl-L-isoleucyl-L-arginyl-L- α -aspartyl-L-
 arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

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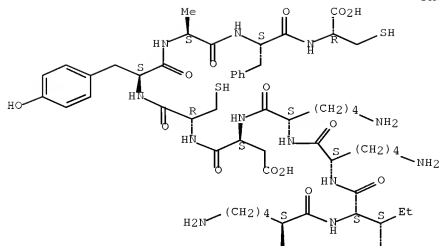


RN 496953-53-8 CAPLUS

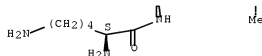
CN L-Cysteine, L-lysyl-L-lysyl-L-isoleucyl-L-lysyl-L-lysyl-L- α -aspartyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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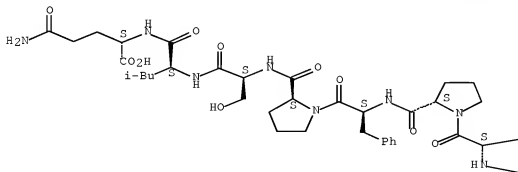


RN 496953-54-9 CAPLUS

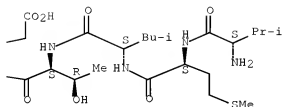
CN L-Glutamine, L-valyl-L-methionyl-L-leucyl-L-threonyl-L- α -aspartyl-L-prolyl-L-phenylalanyl-L-prolyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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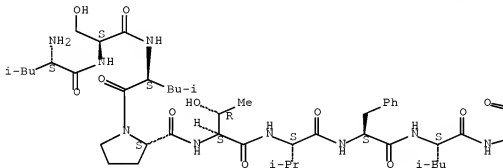


RN 496953-55-0 CAPLUS

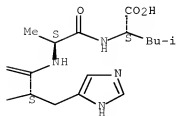
CN L-Leucine, L-leucyl-L-seryl-L-leucyl-L-prolyl-L-threonyl-L-valyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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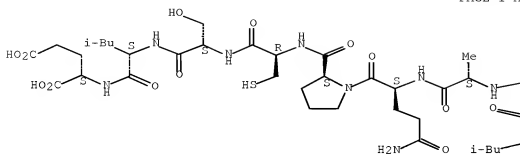
RN 496953-56-1 CAPLUS

CN L-Glutamic acid, L-phenylalanyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl-L-glutamyl-L-prolyl-L-cysteinyl-L-seryl-L-leucyl- (9CI) (CA

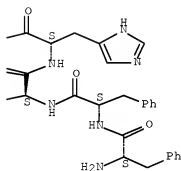
INDEX NAME)

Absolute stereochemistry.

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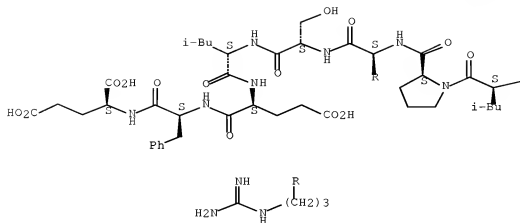


RN 496953-57-2 CAPLUS

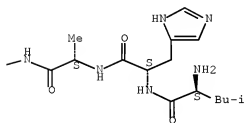
CN L-Glutamic acid, L-leucyl-L-histidyl-L-alanyl-L-leucyl-L-prolyl-L-arginyl-L-seryl-L-leucyl-L- α -glutamyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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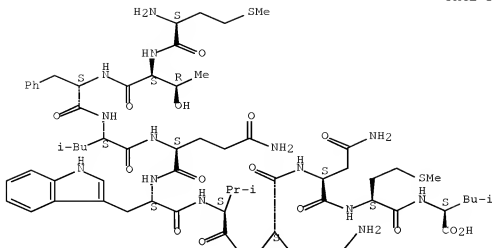


RN 496953-58-3 CAPLUS

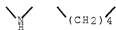
CN L-Leucine, L-methionyl-L-threonyl-L-phenylalanyl-L-leucyl-L-glutaminyll-L-tryptophyl-L-valyl-L-lysyll-L-asparaginyll-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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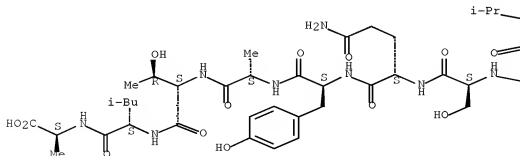


RN 496953-59-4 CAPLUS

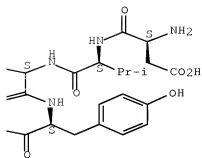
CN L-Alanine, L- α -aspartyl-L-valyl-L-valyl-L-tyrosyl-L-seryl-L-glutamyl-L-tyrosyl-L-alanyl-L-threonyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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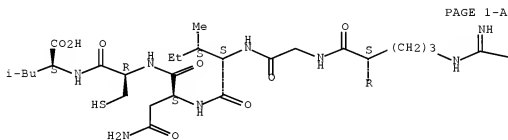
PAGE 1-B



RN 496953-60-7 CAPLUS

CN L-Leucine, L-asparaginyl-L-methionyl-L-valyl-L-phenylalanyl-L-valyl-L-
 arginylglycyl-L-isoleucyl-L-asparaginyl-L-cysteinyl- (9CI) (CA INDEX
 NAME)

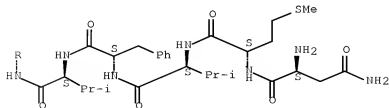
Absolute stereochemistry.



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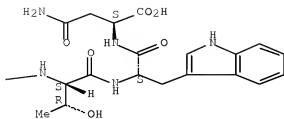
PAGE 2-A



RN 496953-61-8 CAPLUS

CN L-Serine, L-seryl-L-glutaminyl-L- α -glutamyl-L-phenylalanyl-L- α -
 glutamyl-L-valyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-alanyl- (9CI) (CA

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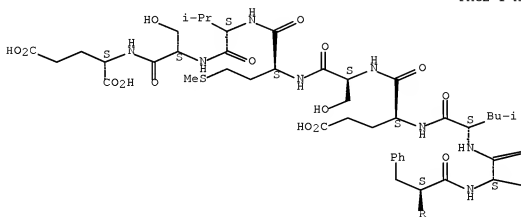


RN 496953-64-1 CAPLUS

CN L-Glutamic acid, L-valyl-L-valyl-L-phenylalanyl-L-seryl-L-leucyl-L- α -glutamyl-L-seryl-L-methionyl-L-valyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

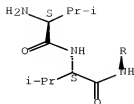
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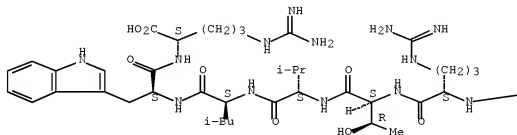


RN 496953-65-2 CAPLUS

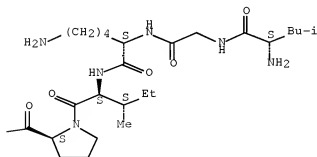
CN L-Arginine, L-leucylglycyl-L-lysyl-L-isoleucyl-L-prolyl-L-arginyl-L-threonyl-L-valyl-L-leucyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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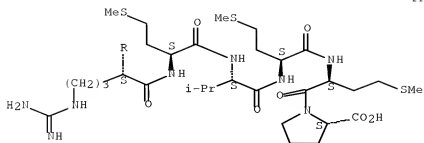


RN 496953-66-3 CAPLUS

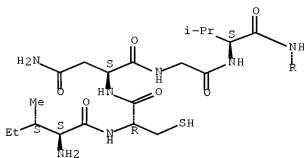
CN Glycine, L-valyl-L-lysyl-L-tryptophyl-L-leucyl-L-prolyl-L-arginyl-L-asparaginyl-L-α-aspartyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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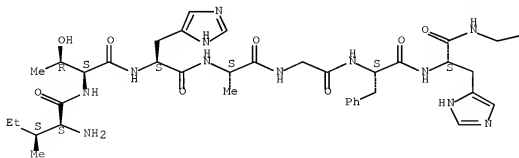


RN 496953-70-9 CAPLUS

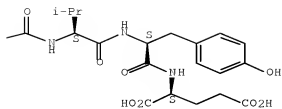
CN L-Glutamic acid, L-isoleucyl-L-threonyl-L-histidyl-L-alanylglycyl-L-phenylalanyl-L-histidylglycyl-L-valyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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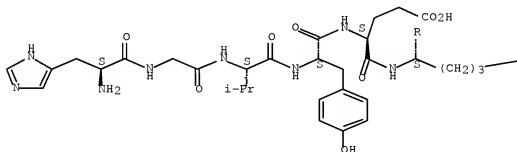


RN 496953-71-0 CAPLUS

CN L-Valine, L-histidylglycyl-L-valyl-L-tyrosyl-L- α -glutamyl-L-arginyl-L-isoleucyl-L-cysteinyl-L-asparaginylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

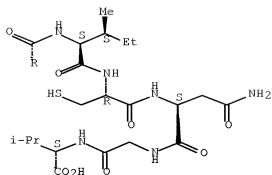
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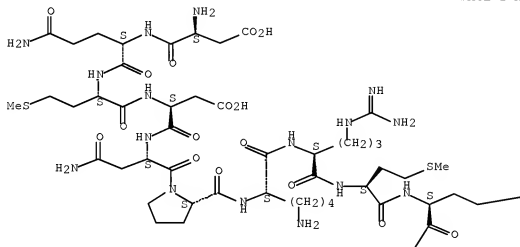


RN 496953-72-1 CAPLUS

CN L-Threonine, L- α -aspartyl-L-glutaminyl-L-methionyl-L- α -
 aspartyl-L-asparaginyl-L-prolyl-L-lysyl-L-arginyl-L-methionyl-L- α -
 glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

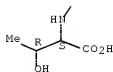
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—CO₂H

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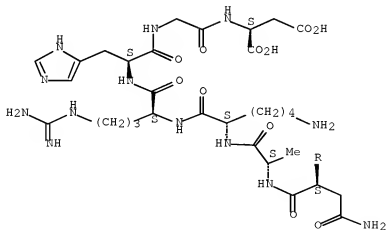


RN 496953-73-2 CAPLUS

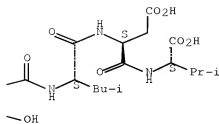
CN L-Aspartic acid, L-methionyl-L- α -aspartyl-L-asparaginyl-L-alanyl-L-lysyl-L-arginyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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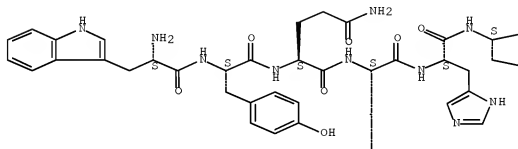


RN 496953-76-5 CAPLUS

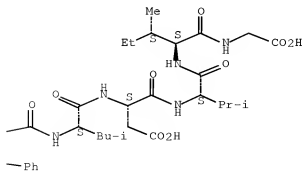
CN Glycine, L-tryptophyl-L-tyrosyl-L-glutaminyl-L-tyrosyl-L-histidyl-L-phenylalanyl-L-leucyl-L- α -aspartyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

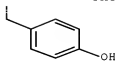
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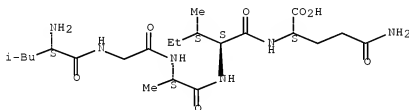
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RN 496953-77-6 CAPLUS

CN L-Glutamine, L-leucylglycyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

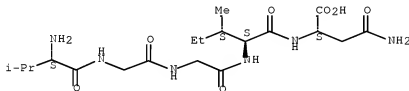
Absolute stereochemistry.



RN 496953-78-7 CAPLUS

CN L-Asparagine, L-valylglycylglycyl-L-isoleucyl- (9CI) (CA INDEX NAME)

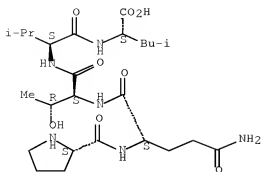
Absolute stereochemistry.



RN 496953-80-1 CAPLUS

CN L-Leucine, L-prolyl-L-glutamyl-L-threonyl-L-valyl- (9CI) (CA INDEX NAME)

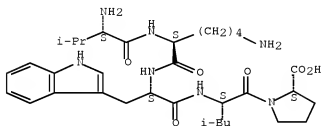
Absolute stereochemistry.



RN 496953-81-2 CAPLUS

CN L-Proline, L-valyl-L-lysyl-L-tryptophyl-L-leucyl- (9CI) (CA INDEX NAME)

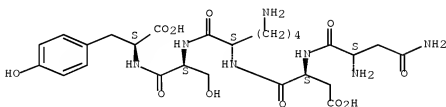
Absolute stereochemistry.



RN 496953-83-4 CAPLUS

CN L-Tyrosine, L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 496953-96-7 496953-88-3 496953-90-3

496953-92-5 496953-94-7 496953-95-3

496953-97-0 496953-98-1 496953-99-2

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496954-04-2 496954-05-3 496954-07-5

496954-09-7

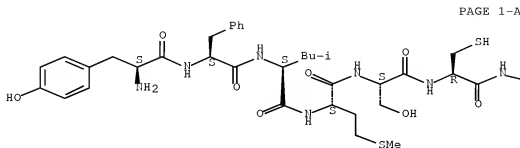
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MDR1 encoding P-glycoprotein)

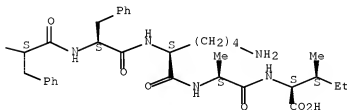
RN 496953-86-7 CAPLUS

CN L-Isoleucine, L-tyrosyl-L-phenylalanyl-L-leucyl-L-methionyl-L-seryl-L-cysteiny-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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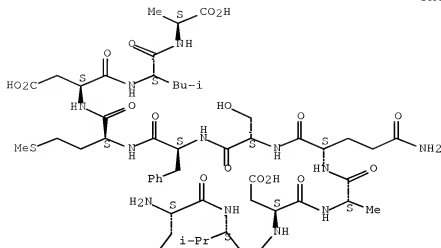


RN 496953-88-9 CAPLUS

CN L-Alanine, L-seryl-L-valyl-L- α -aspartyl-L-alanyl-L-glutaminyl-L-seryl-L-phenylalanyl-L-methionyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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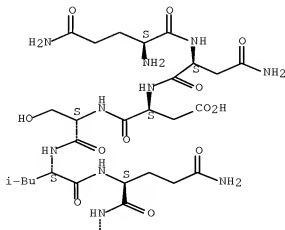


RN 496953-90-3 CAPLUS

CN L-Phenylalanine, L-glutaminyl-L-asparaginyl-L- α -aspartyl-L-seryl-L-leucyl-L-glutaminyl-L- α -glutamyl-L-asparaginyl-L-isoleucyl-L-leucyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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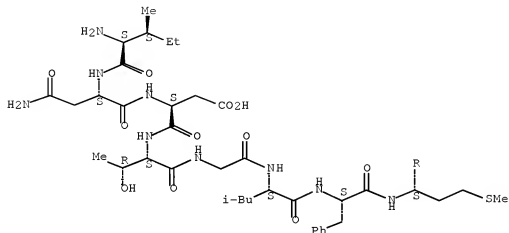


RN 496953-94-7 CAPLUS

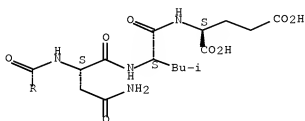
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Absolute stereochemistry.

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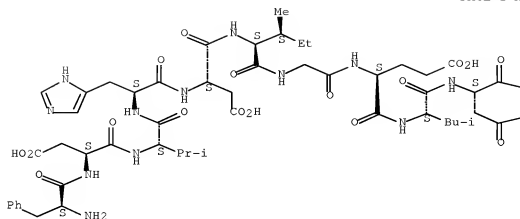


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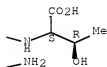
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Absolute stereochemistry.

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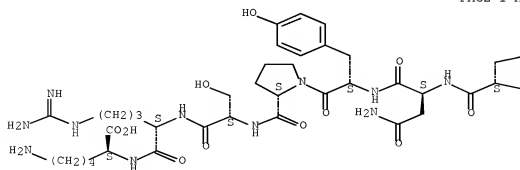


RN 496953-97-0 CAPLUS

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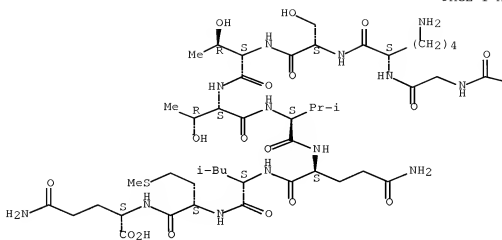
Absolute stereochemistry.

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Absolute stereochemistry.

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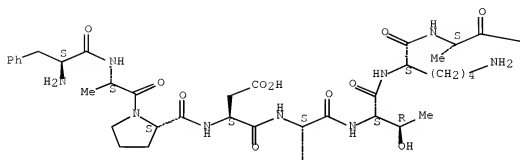


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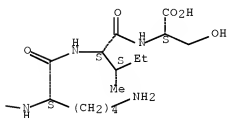
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Absolute stereochemistry.

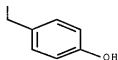
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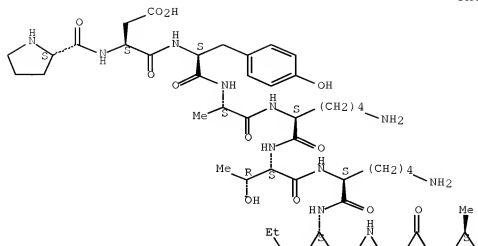


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Absolute stereochemistry.

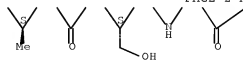
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PAGE 2-B

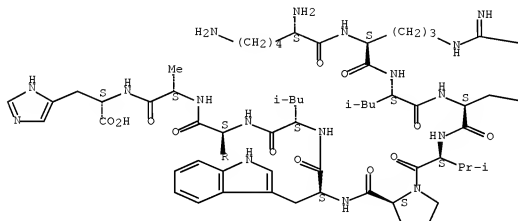


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Absolute stereochemistry.

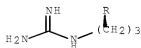
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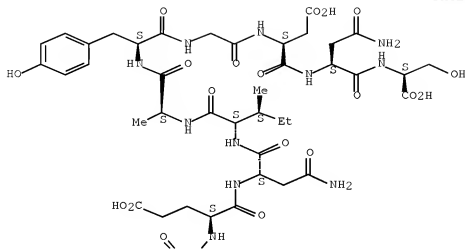
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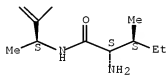
(CA INDEX NAME)

Absolute stereochemistry.

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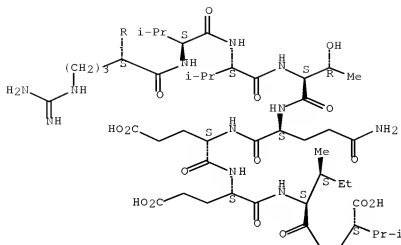


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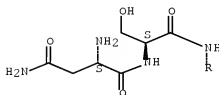
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Absolute stereochemistry.

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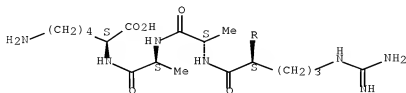


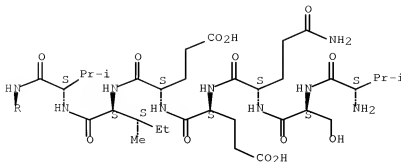
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Absolute stereochemistry.

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L80 ANSWER 16 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:133047 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:163518

TITLE: Improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5

INVENTOR(S): Heinrich, Guenther; Kerb, Reinhold

PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013534	A2	20030220	WO 2002-EP8219	20020723 <--
WO 2003013534	A3	20031009		
WO 2003013534	A9	20040429		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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PRIORITY APPLN. INFO.:			EP 2001-117608	A 20010723 <--
			EP 2002-11710	A 20020524 <--
			WO 2002-EP8219	W 20020723 <--

AB The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with

variant alleles of genes involved in irinotecan metabolism, and in particular gene CYP3A5 encoding cytochrome P 450 3A5. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.

- IC ICM A61K031-4741
ICS A61P035-00
- CC 1-6 (Pharmacology)
Section cross-reference(s): 3
- IT Uterus, neoplasm
(cervix; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)
- IT Intestine, neoplasm
(colorectal; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)
- IT Animals
Antitumor agents
Drug resistance
Genotyping (method)
Human
Lung, neoplasm
Mus
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)
- IT 496954-10-0 496954-11-1 497033-22-4 497033-23-5
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)
- IT 496953-51-6 496953-52-7 496953-53-8
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497033-04-2 497033-05-3
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UDP glucosyltransferase 1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

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RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
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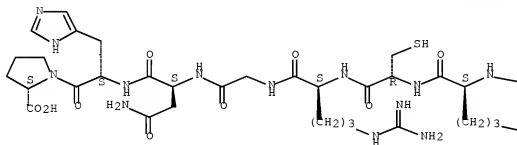
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 (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA topoisomerase I allele fragment; improved treatment of cancer with
 irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome
 P 450 3A5)

RN 496954-10-0 CAPLUS

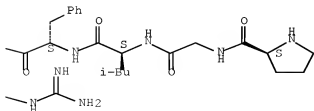
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Absolute stereochemistry.

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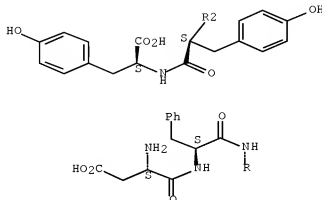


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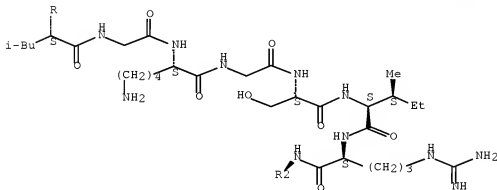
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Absolute stereochemistry.

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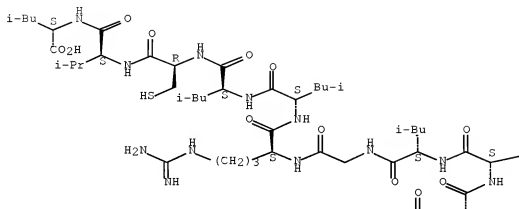


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 RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (UDP glucosyltransferase 1 allele fragment; improved treatment of
 cancer with irinotecan based on genotyping of human gene CYP3A5
 encoding cytochrome P 450 3A5)
 RN 496953-51-6 CAPLUS
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Absolute stereochemistry.

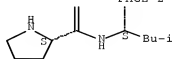
PAGE 1-A



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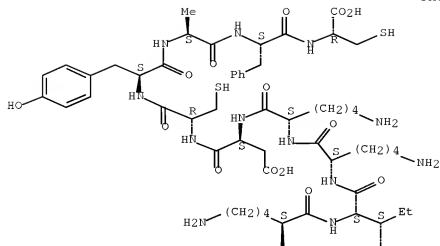
PAGE 2-A



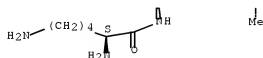
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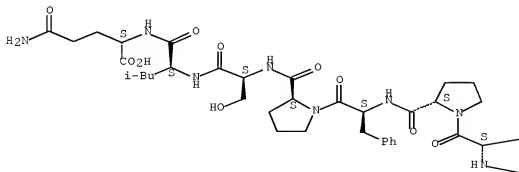


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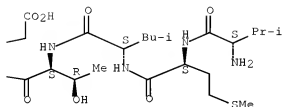
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Absolute stereochemistry.

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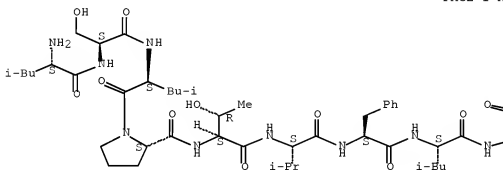


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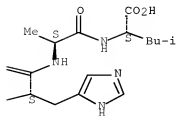
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Absolute stereochemistry.

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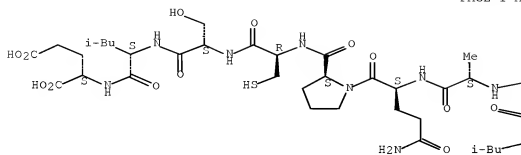
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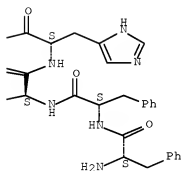
INDEX NAME)

Absolute stereochemistry.

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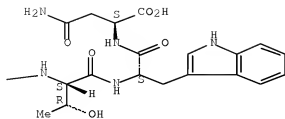


RN 496953-57-2 CAPLUS

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Absolute stereochemistry.

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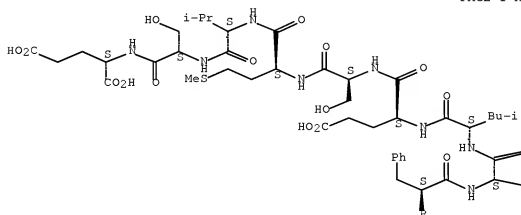


RN 496953-64-1 CAPLUS

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Absolute stereochemistry.

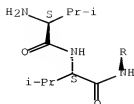
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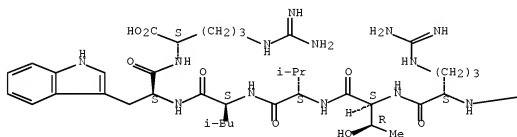


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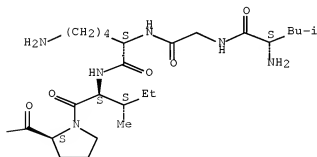
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Absolute stereochemistry.

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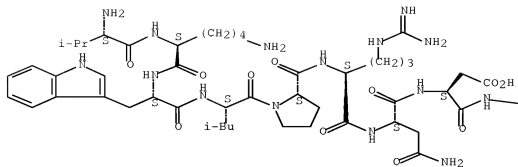


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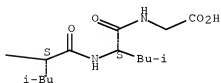
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Absolute stereochemistry.

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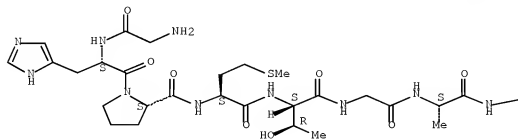


RN 496953-67-4 CAPLUS

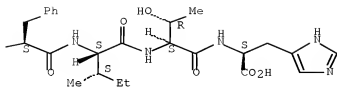
CN L-Histidine, glycyl-L-histidyl-L-prolyl-L-methionyl-L-threonylglycyl-L-alanyl-L-phenylalanyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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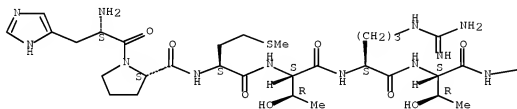


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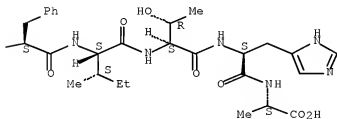
CN L-Alanine, L-histidyl-L-prolyl-L-methionyl-L-threonyl-L-arginyl-L-threonyl-L-phenylalanyl-L-isoleucyl-L-threonyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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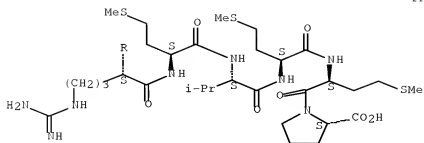


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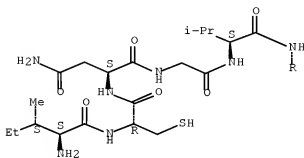
CN L-Proline, L-isoleucyl-L-cysteinyl-L-asparaginylglycyl-L-valyl-L-arginyl-L-methionyl-L-valyl-L-methionyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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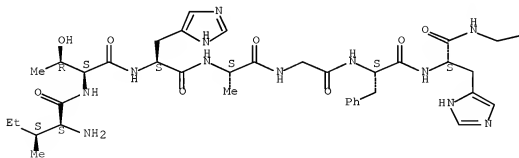


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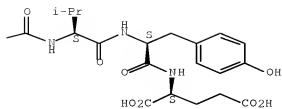
CN L-Glutamic acid, L-isoleucyl-L-threonyl-L-histidyl-L-alanylglycyl-L-phenylalanyl-L-histidylglycyl-L-valyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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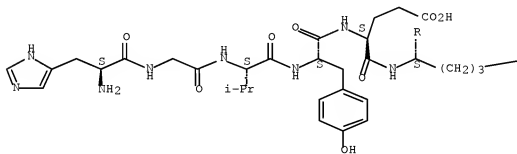


RN 496953-71-0 CAPLUS

CN L-Valine, L-histidylglycyl-L-valyl-L-tyrosyl-L- α -glutamyl-L-arginyl-L-isoleucyl-L-cysteinyl-L-asparaginylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

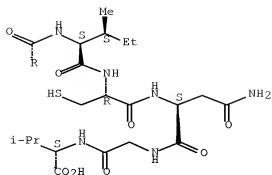
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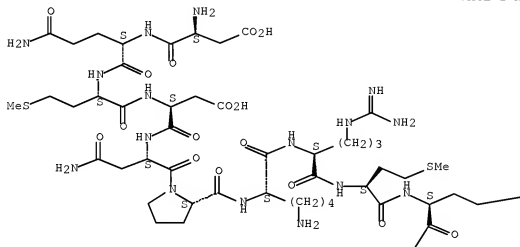


RN 496953-72-1 CAPLUS

CN L-Threonine, L- α -aspartyl-L-glutaminyl-L-methionyl-L- α -
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 glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

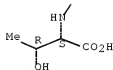
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—CO₂H

PAGE 2-A

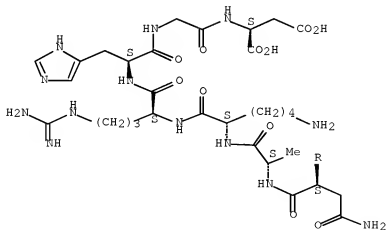


RN 496953-73-2 CAPLUS

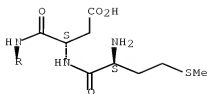
CN L-Aspartic acid, L-methionyl-L- α -aspartyl-L-asparaginyl-L-alanyl-L-lysyl-L-arginyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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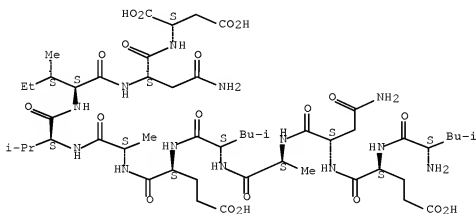
PAGE 2-A



RN 496953-74-3 CAPLUS

CN L-Aspartic acid, L-leucyl-L- α -glutamyl-L-asparaginyl-L-alanyl-L-leucyl-L- α -glutamyl-L-alanyl-L-valyl-L-isoleucyl-L-asparaginyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

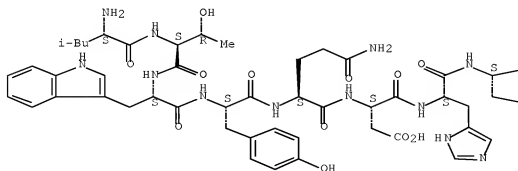


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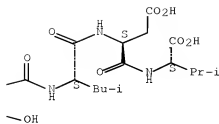
CN L-Valine, L-leucyl-L-threonyl-L-tryptophyl-L-tyrosyl-L-glutamyl-L- α -aspartyl-L-histidyl-L-seryl-L-leucyl-L- α -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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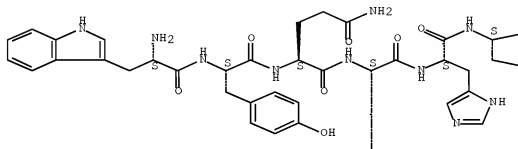


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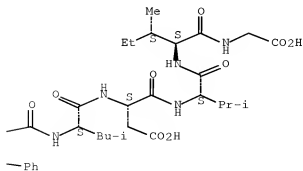
CN Glycine, L-tryptophyl-L-tyrosyl-L-glutaminyl-L-tyrosyl-L-histidyl-L-phenylalanyl-L-leucyl-L- α -aspartyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

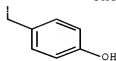
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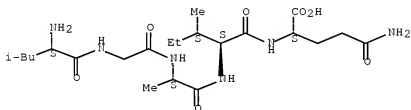
PAGE 2-A



RN 496953-77-6 CAPLUS

CN L-Glutamine, L-leucylglycyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

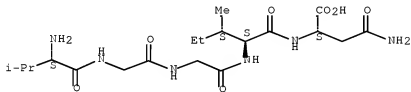
Absolute stereochemistry.



RN 496953-78-7 CAPLUS

CN L-Asparagine, L-valylglycylglycyl-L-isoleucyl- (9CI) (CA INDEX NAME)

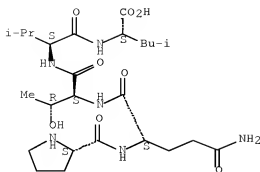
Absolute stereochemistry.



RN 496953-80-1 CAPLUS

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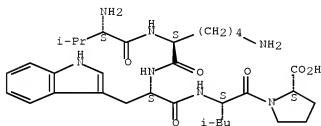
Absolute stereochemistry.



RN 496953-81-2 CAPLUS

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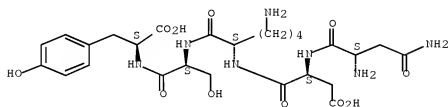
Absolute stereochemistry.



RN 496953-83-4 CAPLUS

CN L-Tyrosine, L-asparaginyl-L-α-aspartyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 496953-96-7 496953-88-3 496953-90-3

496953-92-5 496953-94-7 496953-95-3

496953-97-0 496953-98-1 496953-99-2

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496954-09-7

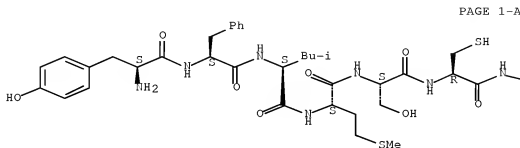
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

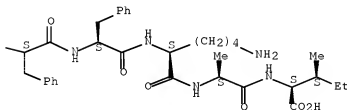
RN 496953-86-7 CAPLUS

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Absolute stereochemistry.



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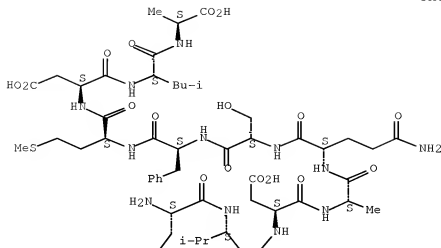


RN 496953-88-9 CAPLUS

CN L-Alanine, L-seryl-L-valyl-L- α -aspartyl-L-alanyl-L-glutaminy-L-seryl-L-phenylalanyl-L-methionyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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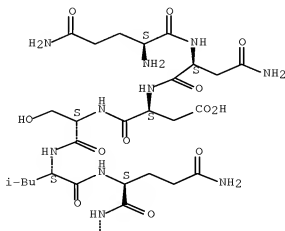


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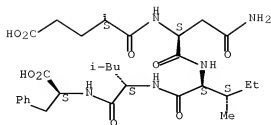
CN L-Phenylalanine, L-glutaminyl-L-asparaginyl-L-α-aspartyl-L-seryl-L-leucyl-L-glutaminyl-L-α-glutamyl-L-asparaginyl-L-isoleucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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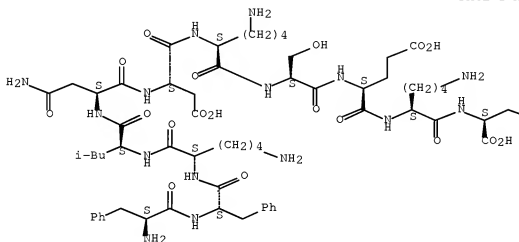


RN 496953-92-5 CAPLUS

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Absolute stereochemistry.

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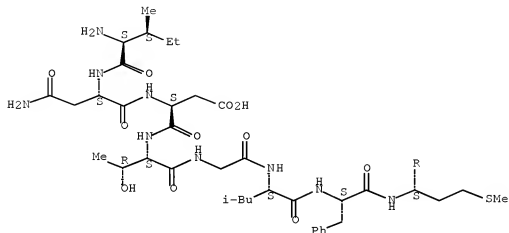
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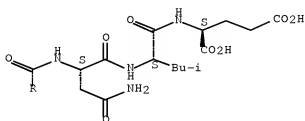
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Absolute stereochemistry.

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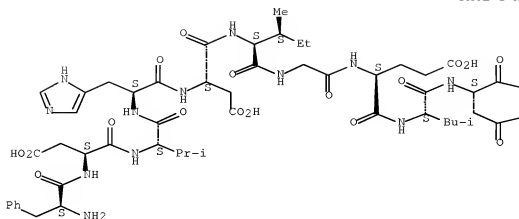


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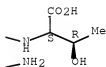
CN L-Threonine, L-phenylalanyl-L- α -aspartyl-L-valyl-L-histidyl-L- α -aspartyl-L-isoleucylglycyl-L- α -glutamyl-L-leucyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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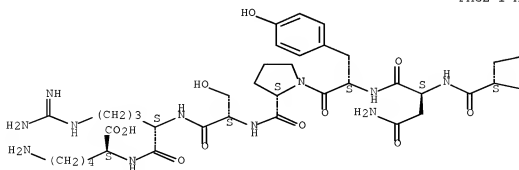


RN 496953-97-0 CAPLUS

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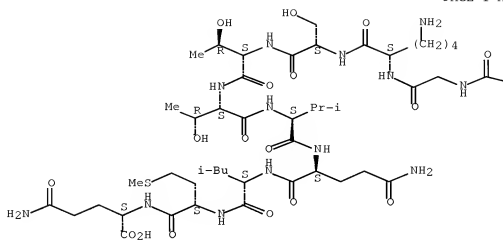
Absolute stereochemistry.

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Absolute stereochemistry.

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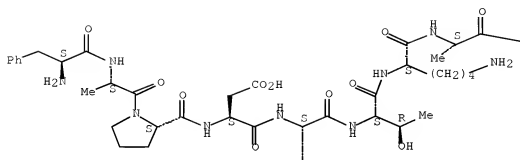


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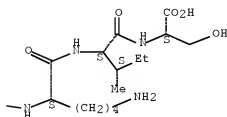
CN L-Threonine, L-lysyl-L- α -glutamyl-L-leucyl-L- α -glutamylglycyl-L-serylglycyl-L-lysyl-L-isoleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

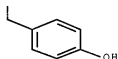
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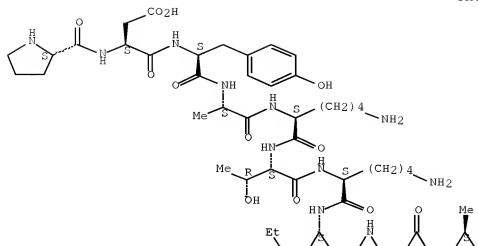


RN 496954-02-0 CAPLUS

CN L-Alanine, L-prolyl-L- α -aspartyl-L-tyrosyl-L-alanyl-L-lysyl-L-threonyl-L-lysyl-L-isoleucyl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

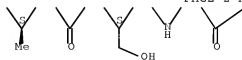
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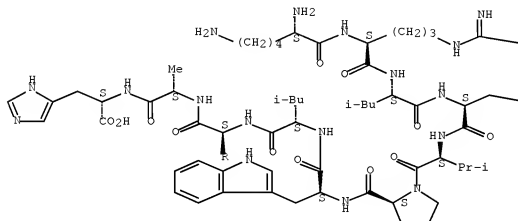


RN 496954-04-2 CAPLUS

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Absolute stereochemistry.

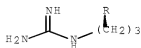
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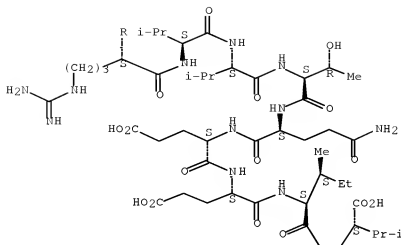
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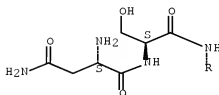
RN 496954-05-3 CAPLUS

CN L-Serine, L-isoleucyl-L-alanyl-L-α-glutamyl-L-asparaginyl-L-isoleucyl-L-alanyl-L-tyrosylglycyl-L-α-aspartyl-L-asparaginyl- (9CI)

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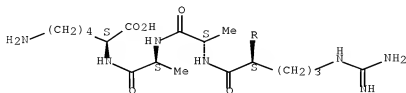


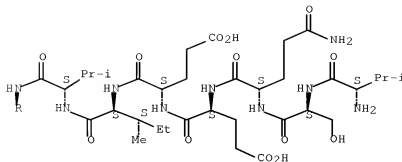
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CN L-Lysine, L-valyl-L-seryl-L-glutamyl-L- α -glutamyl-L- α -glutamyl-L-isoleucyl-L-valyl-L-arginyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L80 ANSWER 17 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:133046 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:163517

TITLE: Improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1

INVENTOR(S): Heinrich, Guenther; Kerb, Reinhold

PATENT ASSIGNEE(S): Epidauros Biotechnologie AG, Germany

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013533	A2	20030220	WO 2002-EP8200	20020723 <--
WO 2003013533	A3	20031009		
WO 2003013533	A9	20040429		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 20050032724	A1	20050210	US 2004-484577	20040812 <--
PRIORITY APPLN. INFO.:				
				A 20010723 <--
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				WO 2002-EP8200 W 20020723 <--

AB The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, gastric cancer, lung cancer, malignant glioma,

ovarian cancer, and pancreatic cancer in a patient having a genotype with variant alleles of genes involved in irinotecan metabolism, in particular the multidrug resistance protein 1 gene MRP1. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.

IC ICM A61K031-4741
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3
IT Uterus, neoplasm
(cervix; improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1)
IT Intestine, neoplasm
(colorectal; improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1)
IT Animals
Antitumor agents
Drug resistance
Genotyping (method)
Human
Lung, neoplasm
Mus
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1)
IT 496954-10-0 496954-11-1 497118-42-0 497118-43-1
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1)
IT 496953-51-6 496953-52-7 496953-53-8
496953-54-9 496953-55-0 496953-56-1
496953-57-2 496953-58-3 496953-59-4
496953-60-7 496953-61-8 496953-62-0
496953-64-1 496953-65-2 496953-66-3
496953-67-4 496953-68-5 496953-69-6
496953-70-9 496953-71-0 496953-72-1
496953-73-2 496953-74-3 496953-75-4
496953-76-5 496953-77-6 496953-78-7
496953-79-8 496953-80-1 496953-81-2
496953-83-4 497117-94-9 497117-95-0 497117-96-1
497117-97-2 497117-99-4 497118-00-0 497118-01-1 497118-02-2
497118-04-4 497118-05-5 497118-06-6 497118-07-7 497118-09-9
497118-10-2 497118-11-3 497118-12-4 497118-14-6 497118-15-7
497118-16-8 497118-17-9 497118-18-0 497118-19-1 497118-20-4
497118-21-5 497118-23-7
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UDP glucosyltransferase 1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding

multidrug resistance protein 1)

IT 496953-86-7 496953-88-9 496953-90-3
 496953-92-5 496953-94-7 496953-95-8
 496953-97-0 496953-98-1 496953-99-2
 496954-00-8 496954-01-3 496954-02-0
 496954-04-2 496954-05-3 496954-07-5
 496954-09-7 497118-24-8 497118-25-9 497118-26-0
 497118-27-1 497118-28-2 497118-29-3 497118-30-6 497118-31-7
 497118-32-8 497118-33-9 497118-35-1 497118-36-2 497118-37-3
 497118-38-4 497118-40-8 497118-41-9

RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (multidrug resistance protein MRP1 allele fragment; improved
 treatment of cancer with irinotecan based on genotyping of human gene
 MRP1 encoding multidrug resistance protein 1)

IT 496954-10-0 496954-11-1

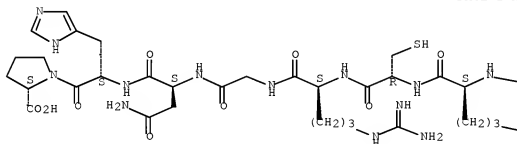
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST
 (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA topoisomerase I allele fragment; improved treatment of cancer with
 irinotecan based on genotyping of human gene MRP1 encoding multidrug
 resistance protein 1)

RN 496954-10-0 CAPLUS

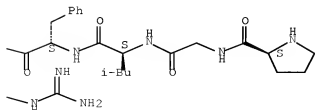
CN L-Proline, L-prolylglycyl-L-leucyl-L-phenylalanyl-L-arginyl-L-cysteinyl-L-
 arginylglycyl-L-asparaginy-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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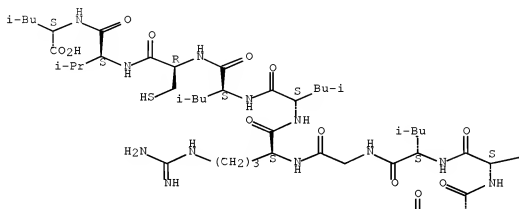
PAGE 1-B



CN L-Leucine, L-prolyl-L-leucyl-L-valyl-L-leucylglycyl-L-arginyl-L-leucyl-L-leucyl-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

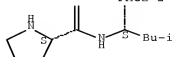
PAGE 1-A



PAGE 1-B

Pr-i

PAGE 2-A

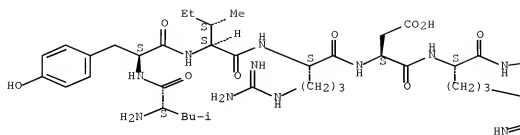


RN 496953-52-7 CAPLUS

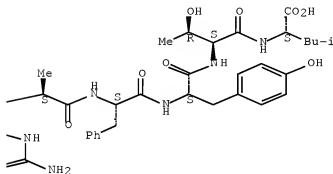
CN L-Leucine, L-leucyl-L-tyrosyl-L-isoleucyl-L-arginyl-L- α -aspartyl-L-arginyl-L-alanyl-L-phenylalanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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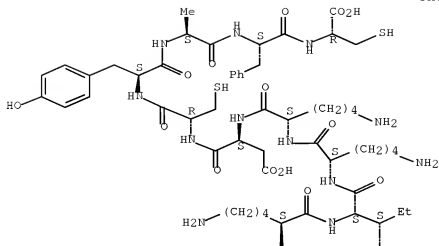


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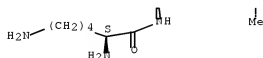
CN L-Cysteine, L-lysyl-L-lysyl-L-isoleucyl-L-lysyl-L-lysyl-L- α -aspartyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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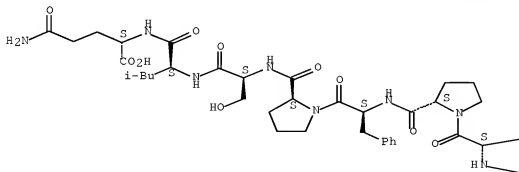


RN 496953-54-9 CAPLUS

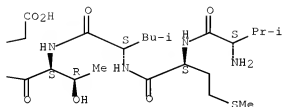
CN L-Glutamine, L-valyl-L-methionyl-L-leucyl-L-threonyl-L- α -aspartyl-L-prolyl-L-phenylalanyl-L-prolyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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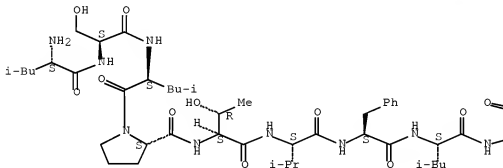


RN 496953-55-0 CAPLUS

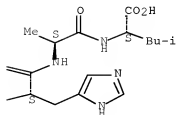
CN L-Leucine, L-leucyl-L-seryl-L-leucyl-L-prolyl-L-threonyl-L-valyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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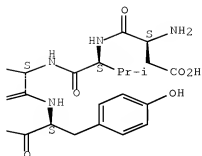
PAGE 1-B



RN 496953-56-1 CAPLUS

CN L-Glutamic acid, L-phenylalanyl-L-phenylalanyl-L-leucyl-L-histidyl-L-alanyl-L-glutamyl-L-prolyl-L-cysteinyl-L-seryl-L-leucyl- (9CI) (CA

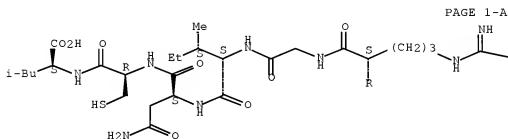
PAGE 1-B



RN 496953-60-7 CAPLUS

CN L-Leucine, L-asparaginyl-L-methionyl-L-valyl-L-phenylalanyl-L-valyl-L-
 arginylglycyl-L-isoleucyl-L-asparaginyl-L-cysteinyl- (9CI) (CA INDEX
 NAME)

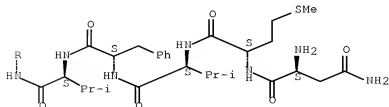
Absolute stereochemistry.



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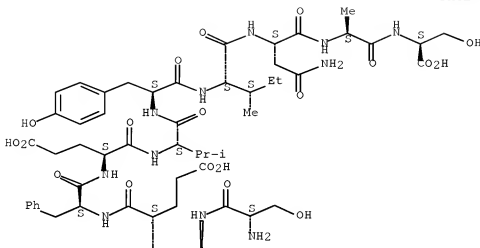
RN 496953-61-8 CAPLUS

CN L-Serine, L-seryl-L-glutaminyl-L- α -glutamyl-L-phenylalanyl-L- α -
 glutamyl-L-valyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-alanyl- (9CI) (CA

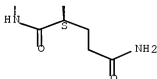
INDEX NAME)

Absolute stereochemistry.

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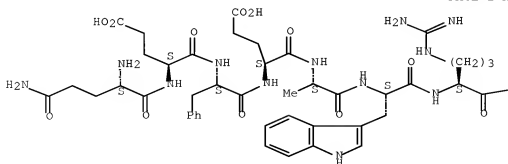


RN 496953-63-0 CAPLUS

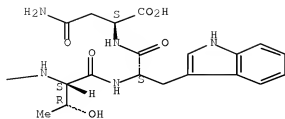
CN L-Asparagine, L-glutaminyl-L- α -glutamyl-L-phenylalanyl-L- α -glutamyl-L-alanyl-L-tryptophyl-L-arginyl-L-threonyl-L-tryptophyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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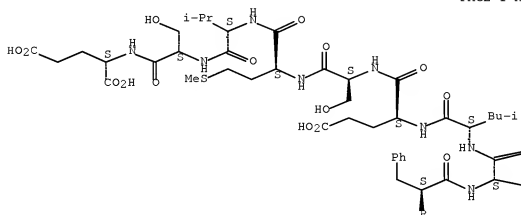


RN 496953-64-1 CAPLUS

CN L-Glutamic acid, L-valyl-L-valyl-L-phenylalanyl-L-seryl-L-leucyl-L- α -glutamyl-L-seryl-L-methionyl-L-valyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

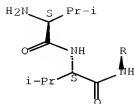
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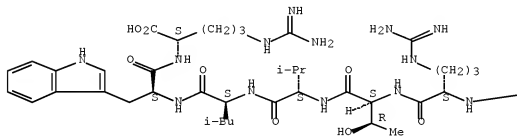


RN 496953-65-2 CAPLUS

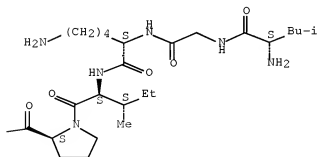
CN L-Arginine, L-leucylglycyl-L-lysyl-L-isoleucyl-L-prolyl-L-arginyl-L-threonyl-L-valyl-L-leucyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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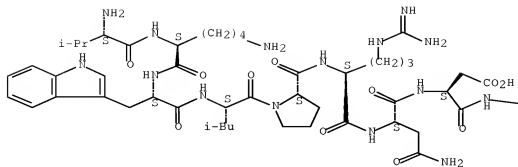


RN 496953-66-3 CAPLUS

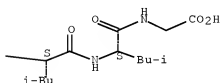
CN Glycine, L-valyl-L-lysyl-L-tryptophyl-L-leucyl-L-prolyl-L-arginyl-L-asparaginyl-L-α-aspartyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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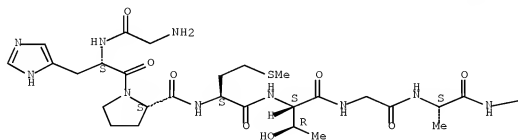


RN 496953-67-4 CAPLUS

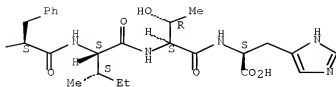
CN L-Histidine, glycyl-L-histidyl-L-prolyl-L-methionyl-L-threonylglycyl-L-alanyl-L-phenylalanyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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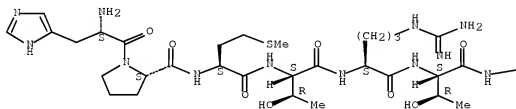


RN 496953-68-5 CAPLUS

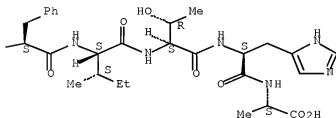
CN L-Alanine, L-histidyl-L-prolyl-L-methionyl-L-threonyl-L-arginyl-L-threonyl-L-phenylalanyl-L-isoleucyl-L-threonyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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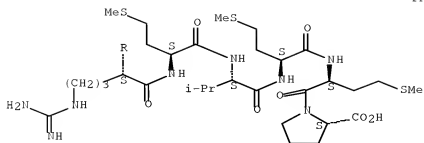


RN 496953-69-6 CAPLUS

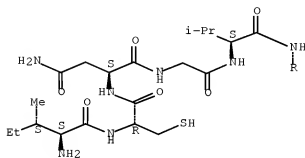
CN L-Proline, L-isoleucyl-L-cysteinyl-L-asparaginylglycyl-L-valyl-L-arginyl-L-methionyl-L-valyl-L-methionyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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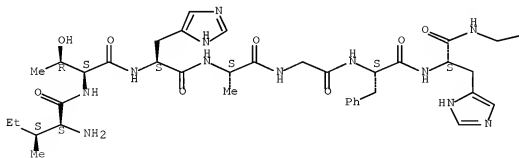


RN 496953-70-9 CAPLUS

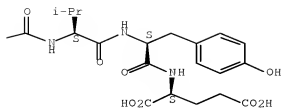
CN L-Glutamic acid, L-isoleucyl-L-threonyl-L-histidyl-L-alanylglycyl-L-phenylalanyl-L-histidylglycyl-L-valyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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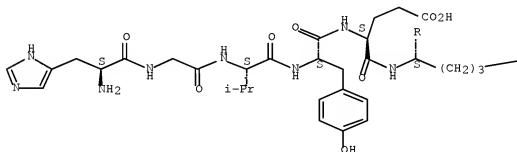


RN 496953-71-0 CAPLUS

CN L-Valine, L-histidylglycyl-L-valyl-L-tyrosyl-L- α -glutamyl-L-arginyl-L-isoleucyl-L-cysteinyl-L-asparaginyglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

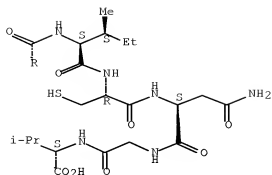
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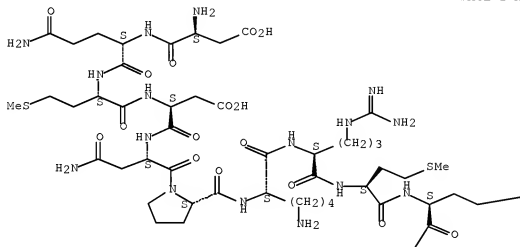


RN 496953-72-1 CAPLUS

CN L-Threonine, L- α -aspartyl-L-glutaminyl-L-methionyl-L- α -
 aspartyl-L-asparaginyl-L-prolyl-L-lysyl-L-arginyl-L-methionyl-L- α -
 glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

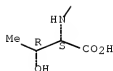
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—CO₂H

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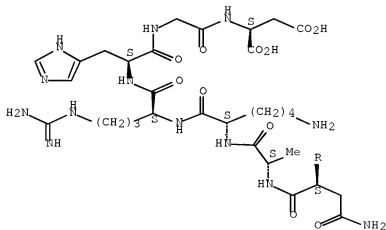


RN 496953-73-2 CAPLUS

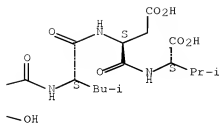
CN L-Aspartic acid, L-methionyl-L- α -aspartyl-L-asparaginyl-L-alanyl-L-lysyl-L-arginyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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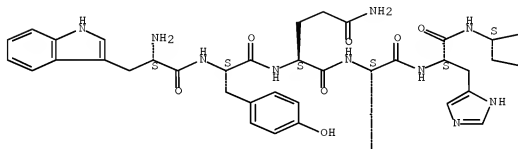


RN 496953-76-5 CAPLUS

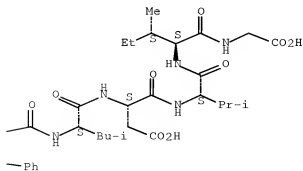
CN Glycine, L-tryptophyl-L-tyrosyl-L-glutaminyl-L-tyrosyl-L-histidyl-L-phenylalanyl-L-leucyl-L- α -aspartyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

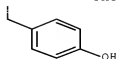
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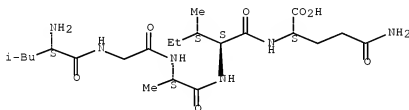
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RN 496953-77-6 CAPLUS

CN L-Glutamine, L-leucylglycyl-L-alanyl-L-isoleucyl- (9CI) (CA INDEX NAME)

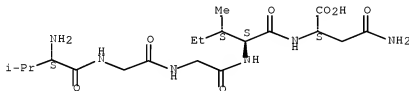
Absolute stereochemistry.



RN 496953-78-7 CAPLUS

CN L-Asparagine, L-valylglycylglycyl-L-isoleucyl- (9CI) (CA INDEX NAME)

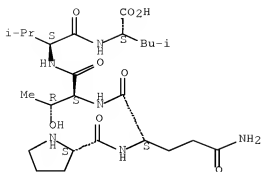
Absolute stereochemistry.



RN 496953-80-1 CAPLUS

CN L-Leucine, L-prolyl-L-glutamyl-L-threonyl-L-valyl- (9CI) (CA INDEX NAME)

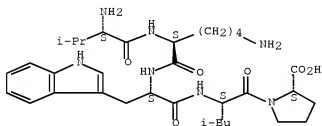
Absolute stereochemistry.



RN 496953-81-2 CAPLUS

CN L-Proline, L-valyl-L-lysyl-L-tryptophyl-L-leucyl- (9CI) (CA INDEX NAME)

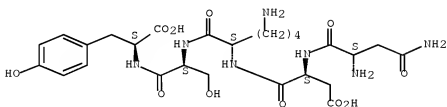
Absolute stereochemistry.



RN 496953-83-4 CAPLUS

CN L-Tyrosine, L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 496953-96-7 496953-88-3 496953-90-3

496953-92-5 496953-94-7 496953-95-3

496953-97-0 496953-98-1 496953-99-2

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496954-04-2 496954-05-3 496954-07-5

496954-09-7

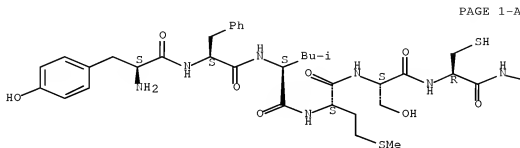
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene MRP1 encoding multidrug resistance protein 1)

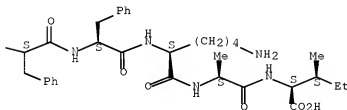
RN 496953-86-7 CAPLUS

CN L-Isoleucine, L-tyrosyl-L-phenylalanyl-L-leucyl-L-methionyl-L-seryl-L-cysteiny-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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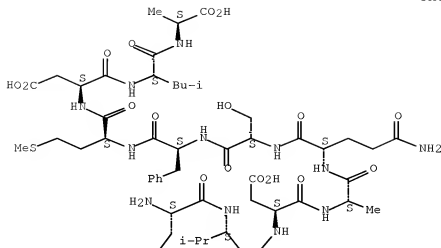


RN 496953-88-9 CAPLUS

CN L-Alanine, L-seryl-L-valyl-L- α -aspartyl-L-alanyl-L-glutaminy-L-seryl-L-phenylalanyl-L-methionyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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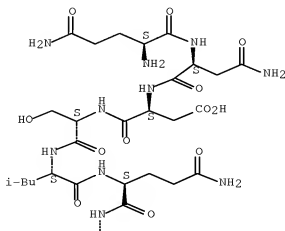


RN 496953-90-3 CAPLUS

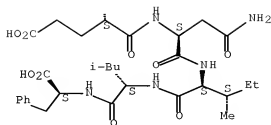
CN L-Phenylalanine, L-glutaminyl-L-asparaginyl-L- α -aspartyl-L-seryl-L-leucyl-L-glutamyl-L- α -glutamyl-L-asparaginyl-L-isoleucyl-L-leucyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

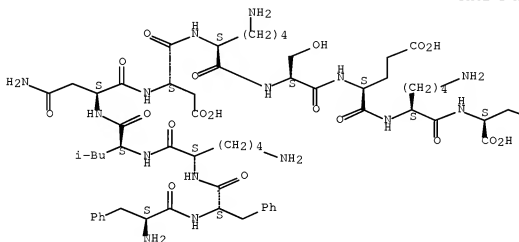


RN 496953-92-5 CAPLUS

CN L-Aspartic acid, L-phenylalanyl-L-phenylalanyl-L-lysyl-L-leucyl-L-asparaginyl-L- α -aspartyl-L-lysyl-L-seryl-L- α -glutamyl-L-lysyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



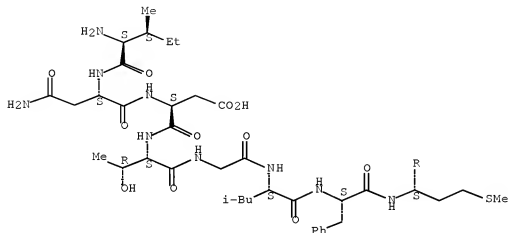
PAGE 1-B

RN 496953-94-7 CAPLUS

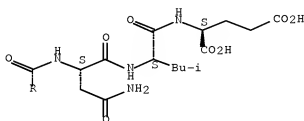
CN L-Glutamic acid, L-isoleucyl-L-asparaginyl-L- α -aspartyl-L-threonylglycyl-L-leucyl-L-phenylalanyl-L-methionyl-L-asparaginyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

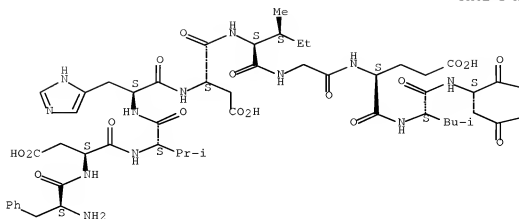


RN 496953-95-8 CAPLUS

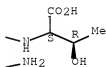
CN L-Threonine, L-phenylalanyl-L- α -aspartyl-L-valyl-L-histidyl-L- α -aspartyl-L-isoleucylglycyl-L- α -glutamyl-L-leucyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

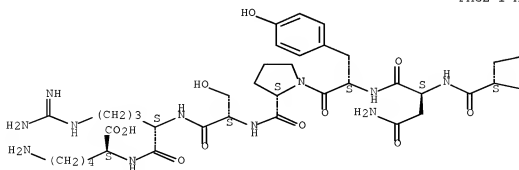


RN 496953-97-0 CAPLUS

CN L-Lysine, L-arginyl-L-asparaginyl-L-valyl-L-histidyl-L-phenylalanyl-L-asparaginyl-L-tyrosyl-L-prolyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)

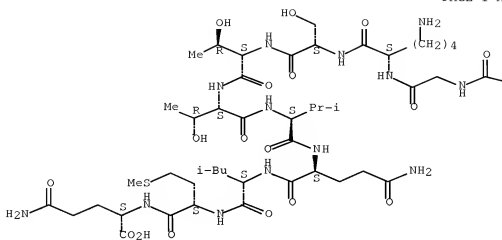
Absolute stereochemistry.

PAGE 1-A



Absolute stereochemistry.

PAGE 1-A



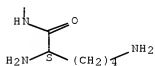
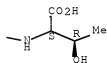
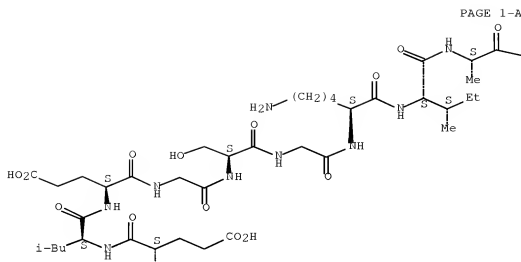
PAGE 1-B



RN 496954-00-8 CAPLUS

CN L-Threonine, L-lysyl-L- α -glutamyl-L-leucyl-L- α -glutamylglycyl-L-serylglycyl-L-lysyl-L-isoleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

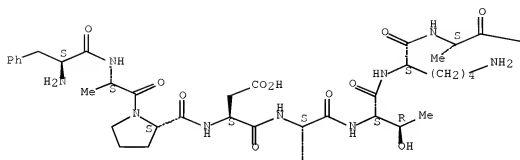


RN 496954-01-9 CAPLUS

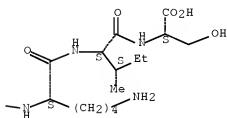
CN L-Serine, L-phenylalanyl-L-alanyl-L-prolyl-L- α -aspartyl-L-tyrosyl-L-threonyl-L-lysyl-L-alanyl-L-lysyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

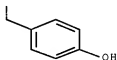
PAGE 1-A



PAGE 1-B



PAGE 2-A

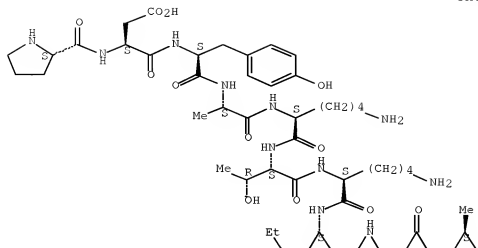


RN 496954-02-0 CAPLUS

CN L-Alanine, L-prolyl-L- α -aspartyl-L-tyrosyl-L-alanyl-L-lysyl-L-threonyl-L-lysyl-L-isoleucyl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

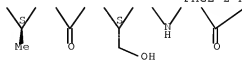
PAGE 1-A



PAGE 1-B



PAGE 2-A



PAGE 2-B

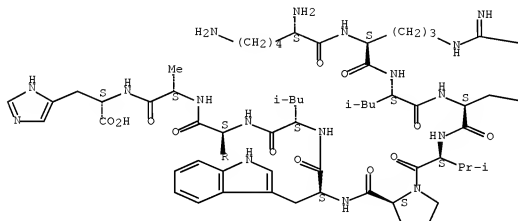


RN 496954-04-2 CAPLUS

CN L-Histidine, L-lysyl-L-arginyl-L-leucyl-L-asparaginyl-L-valyl-L-prolyl-L-tryptophyl-L-leucyl-L-arginyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

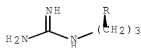
PAGE 1-A



PAGE 1-B



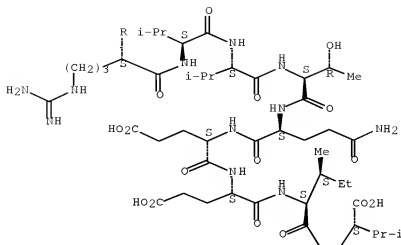
PAGE 2-A



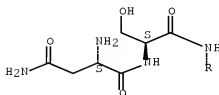
RN 496954-05-3 CAPLUS

CN L-Serine, L-isoleucyl-L-alanyl-L-α-glutamyl-L-asparaginyl-L-isoleucyl-L-alanyl-L-tyrosylglycyl-L-α-aspartyl-L-asparaginyl- (9CI)

PAGE 1-A



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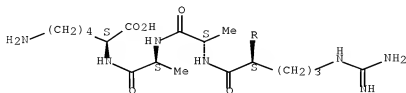


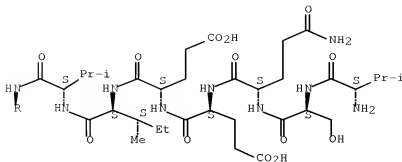
RN 496954-09-7 CAPLUS

CN L-Lysine, L-valyl-L-seryl-L-glutamyl-L- α -glutamyl-L- α -glutamyl-L-isoleucyl-L-valyl-L-arginyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L80 ANSWER 18 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:975688 CAPLUS Full-text

DOCUMENT NUMBER: 138:49910

TITLE: Glutathione-S-transferase (GST)-binding peptides for overcoming antitumor drug resistance and their manufacture

INVENTOR(S): Ando, Toshio; Takahashi, Noriko

PATENT ASSIGNEE(S): Tamaty L.O. K. K., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002371100	A	20021226	JP 2001-176265	20010611 <--
PRIORITY APPLN. INFO.:			JP 2001-176265	20010611 <--

AB The peptides, useful for overcoming antitumor resistance, are manufactured by (1) culturing transformants prepared using plasmid bearing GST gene and purifying GST from the culture, (2) constructing C(X)7C phage library, (3) recovering phages which express GST-binding peptides from the library, (4) purifying the phages from a single plaque, and (5) determining the sequence of the binding peptides. Thirteen specific heptapeptides, e.g. CHWGEPSQC, represented by C(X)7C are also given. The peptides especially inhibit GST π -isozyme of cancer cells and make them susceptible to antitumor drugs.

IC ICM C07K019-00

CC ICS A61P043-00; C12P021-02; A61K038-55; C12N015-09

CC 1-6 (Pharmacology)

Section cross-reference(s): 3, 14, 16

IT Antitumor agents

(resistance to; manufacture of glutathione-S-transferase-binding peptides for overcoming antitumor drug resistance by phage display method)

IT Necroplasm

(treatment of; manufacture of glutathione-S-transferase-binding peptides

for

overcoming antitumor drug resistance by phage display method)

IT 478695-96-6P 478695-99-7P 478696-60-3P

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);

PNC (Pharmacological activity); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(amino acid sequence; manufacture of glutathione-S-transferase-binding peptides for overcoming antitumor drug resistance by phage display method)

IT 478696-01-1P 478696-02-5P 478696-03-6P
478696-04-7P 478696-05-8P 478696-06-9P
478696-07-0P 478696-08-1P

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
PAC (Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(manufacture of glutathione-S-transferase-binding peptides for overcoming antitumor drug resistance by phage display method)

IT 478695-98-6P 478695-99-7P 478696-00-3P

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
PAC (Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

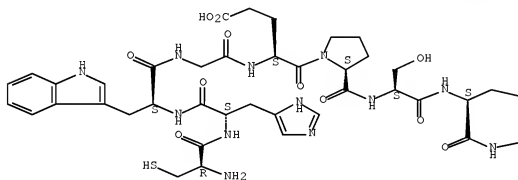
(amino acid sequence; manufacture of glutathione-S-transferase-binding peptides for overcoming antitumor drug resistance by phage display method)

RN 478695-98-6 CAPLUS

CN L-Cysteine, L-cysteinyl-L-histidyl-L-tryptophylglycyl-L- α -glutamyl-L-prolyl-L-seryl-L-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

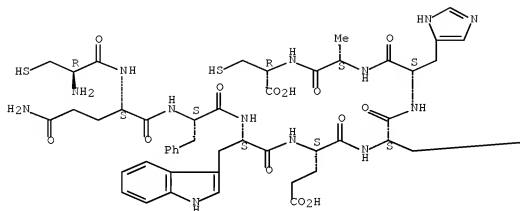


RN 478695-99-7 CAPLUS

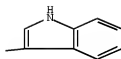
CN L-Cysteine, L-cysteinyl-L-glutaminyl-L-phenylalanyl-L-tryptophyl-L- α -glutamyl-L-tryptophyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

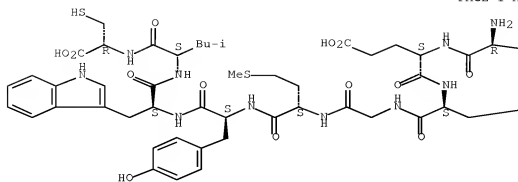


RN 478696-00-3 CAPLUS

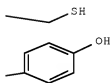
CN L-Cysteine, L-cysteinyl-L- α -glutamyl-L-tyrosylglycyl-L-methionyl-L-tyrosyl-L-tryptophyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT 478696-01-4P 478696-02-5P 478696-03-6P
 478696-04-7P 478696-05-8P 478696-06-9P
 478696-07-0P 478696-08-1P

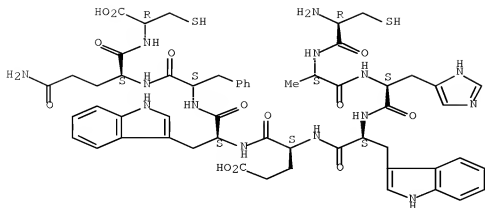
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation);
 PAC (Pharmacological activity); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(manufacture of glutathione-S-transferase-binding peptides for overcoming
 antitumor drug resistance by phage display method)

RN 478696-01-4 CAPLUS

CN L-Cysteine, L-cysteinyl-L-alanyl-L-histidyl-L-tryptophyl-L- α -
 glutamyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

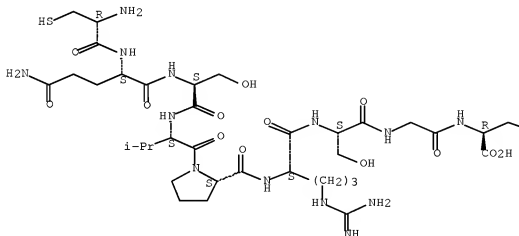


RN 478696-02-5 CAPLUS

CN L-Cysteine, L-cysteiny-L-glutamyl-L-seryl-L-valyl-L-prolyl-L-arginyl-L-serylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

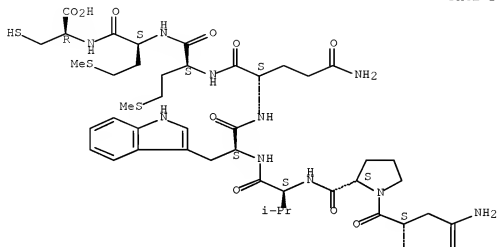
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RN 478696-03-6 CAPLUS

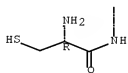
CN L-Cysteine, L-cysteinyl-L-asparaginyl-L-prolyl-L-valyl-L-tryptophyl-L-glutaminyl-L-methionyl-L-methionyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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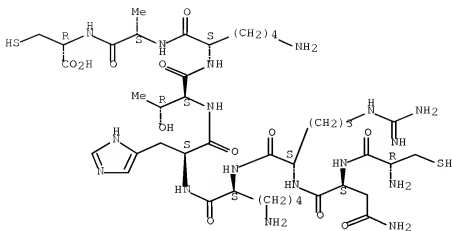
PAGE 2-A



RN 478696-04-7 CAPLUS

CN L-Cysteine, L-cysteinyl-L-asparaginyl-L-arginyl-L-lysyl-L-histidyl-L-threonyl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

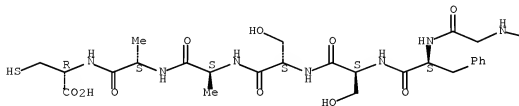


RN 478696-05-8 CAPLUS

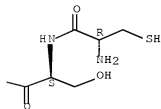
CN L-Cysteine, L-cysteinyl-L-serylglycyl-L-phenylalanyl-L-seryl-L-seryl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

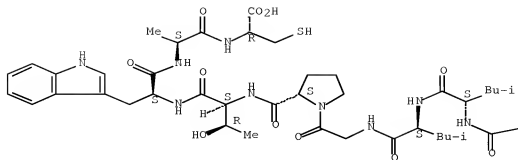


RN 478696-06-9 CAPLUS

CN L-Cysteine, L-cysteinyl-L-leucyl-L-leucylglycyl-L-prolyl-L-threonyl-L-tryptophyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

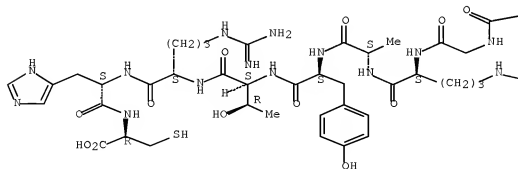


RN 478696-07-0 CAPLUS

CN L-Cysteine, L-cysteinylglycyl-L-arginyl-L-alanyl-L-tyrosyl-L-threonyl-L-arginyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

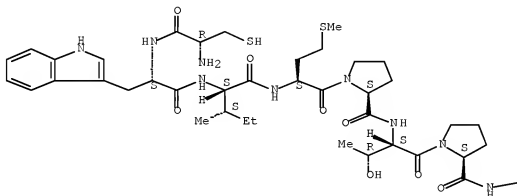


RN 478696-08-1 CAPLUS

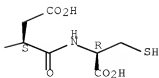
CN L-Cysteine, L-cysteinyl-L-tryptophyl-L-isoleucyl-L-methionyl-L-prolyl-L-threonyl-L-prolyl-L- α -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 19 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:869573 CAPLUS Full-text

DOCUMENT NUMBER: 137:363050

TITLE: Regulating apoptosis in TRAIL-resistant cancer cells, while protecting normal, non-cancerous cells

INVENTOR(S): El-Deiry, Wafik S.; Kim, Kunhong

PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA

SOURCE: U.S. Pat. Appl. Publ., 30 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020169123	A1	20021114	US 2002-85801	20020227 <--
PRIORITY APPLN. INFO.:			US 2001-271674P	P 20010227 <--

AB Provided are compns. and methods for controlling, modulating or regulating extrinsically-induced apoptosis in a population of cells, comprising treating the cell population with a synergistically combined composition comprising an amount of TRAIL in conjunction with an amount of at least one reagent acting on mitochondrial pathways of the cells, which in combination is sufficient to induce cellular apoptosis, such that the apoptosis-inducing effect of the combination is greater than that of TRAIL alone, or the at least one reagent alone, or the additive individual apoptotic effects of TRAIL and the at least one reagent. However, TRAIL-sensitive normal cells are protected from the extrinsically induced apoptosis by treatment with a specific caspase inhibitor, such as a caspase 9 inhibitor. Consequently, in accordance with the present invention, TRAIL-resistant cancer cells are treated and killed with an apoptosis-inducing amount of the TRAIL combination, but the normal cells are protected or rescued from apoptosis by treatment with the specific caspase inhibitor.

IC ICM A61K038-17

INCL 514012000

CC 1-6 (Pharmacology)

Section cross-reference(s): 15

IT Antitumor agents

Apoptosis

Cytoprotective agents

Human

Mitochondria

Neoplasm

Radiotherapy

(regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

IT Antitumor agents

(resistance to; regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

IT 325786-54-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(caspase 9 inhibitor; regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 15663-27-1, Cisplatin 25316-40-9, Adriamycin 33069-62-4, Taxol 33419-42-0, Etoposide 41575-94-4,

Carboplatin 71486-22-1, Vinorelbine. 100286-90-6, CPT11
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

IT 325786-54-7

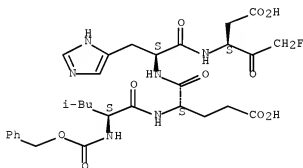
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(caspase 9 inhibitor; regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

RN 325786-54-7 CAPLUS

CN L-Histidinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-L- α -glutamyl-N-
[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT 57-22-7, Vincristine 33069-62-4, Taxol

71486-22-1, Vinorelbine.

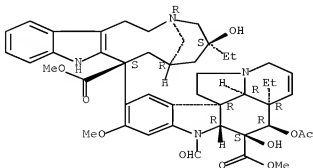
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(regulating apoptosis in TRAIL-resistant cancer cells using TRAIL and reagent acting on mitochondrial pathways while protecting normal non-cancerous cells with caspase inhibitor)

RN 57-22-7 CAPLUS

CN Vincaleukoblastine, 22-oxo- (CA INDEX NAME)

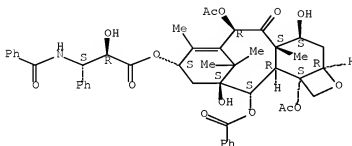
Absolute stereochemistry. Rotation (+).



RN 33069-62-4 CAPLUS

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-,
 (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-
 2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-
 tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl
 ester, (α R, β S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

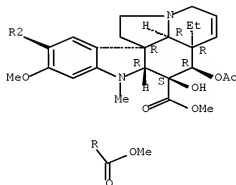


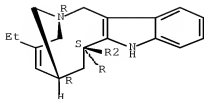
RN 71486-22-1 CAPLUS

CN Aspidospermidine-3-carboxylic acid, 4-(acetyloxy)-6,7-didehydro-15-
 [(2R,6R,8S)-4-ethyl-1,3,6,7,8,9-hexahydro-8-(methoxycarbonyl)-2,6-methano-
 2H-azecino[4,3-b]indol-8-yl]-3-hydroxy-16-methoxy-1-methyl-, methyl ester,
 (2 β ,3 β ,4 β ,5 α ,12R,19 α)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L80 ANSWER 20 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:332057 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 136:335226
 TITLE: Compositions and methods for treating hematologic malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression
 INVENTOR(S): Colgan, Sean P.
 PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA
 SOURCE: PCT Int. Appl., 92 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034291	A2	20020502	WO 2001-US49856	20011025 <--
WO 2002034291	A3	20030530		
W: AU, CA, JP				
RW: AT, BE, CH, PT, SE, TR				
AU 2002031223	A	20020506	AU 2002-31223	20011025 <--
US 20050203036	A1	20050915	US 2001-7255	20011025 <--
US 7105656	B2	20060912		

PRIORITY APPLN. INFO.:
 US 2000-243542P P 20001026 <--
 WO 2001-US49856 W 20011025 <--

AB The invention provides antisense mols. that selectively bind to a hypoxia responsive element (HRE) in the mdrl gene (mdrl-HRE) and, thereby, inhibit transcription of the mdrl gene. The antisense mol. compns. of the invention are useful for treating multidrug resistance associated with various cancers, including those presenting solid tumors and those which do not present solid tumors (hematol. malignancies). This invention is based on the discovery of the nexus between hypoxia and multidrug resistance and the knowledge that cancers which are not associated with solid tumors (e.g., hematol. malignancies such as leukemia) also reportedly exhibit multidrug resistance. The invention provides agents which inhibit hypoxia inducible factor-1 (HIF-1) expression by blocking hif-1 gene expression or the activity of the hif-gene product. Such agents collectively are referred to herein as "HIF-1 binding mols.". The invention further provides a method of screening for agents that modulate the amount of the HIF-1-SUMO-1 complex is provided. A newly discovered small ubiquitin-like-modifier (SUMO-1) appears to antagonize HIF-1 α degradation. The method comprises contacting a HIF-1 mol. with a SUMO-1 mol. under conditions that allow the formation of a HIF-1-SUMO-1 complex, determining the amount of the HIF-1-SUMO-1 complex in the absence of the agent, determining the amount of the HIF-1-SUMO-1 complex in the presence of

the agent, and comparing the amount of the HIF-1-SUMO-1 complex in the presence and absence of the agent.

IC ICM A61K039-395

CC 1-6 (Pharmacology)

Section cross-reference(s): 3

IT Antitumor agents
(hematol.; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

IT Antitumor agents
(leukemia; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

IT Antitumor agents
(lymphoma; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

IT Antitumor agents
(myeloma; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

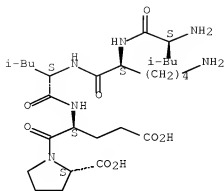
IT 206768-65-2 418763-87-8 418763-88-9
418763-89-0 418763-90-3 418763-91-4
418763-93-6 418763-94-7 418763-95-8
418763-96-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

IT 418763-86-7 418763-92-5
RL: PRP (Properties)
(unclaimed sequence; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

IT 206768-65-2 418763-87-8 418763-88-9
418763-89-0 418763-90-3 418763-91-4
418763-93-6 418763-94-7 418763-95-8
418763-96-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

RN 206768-65-2 CAPUS

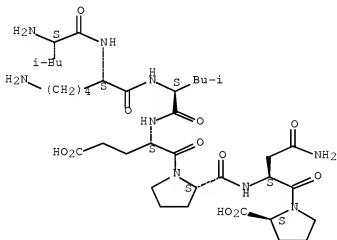
CN Glycine, L-tyrosylglycyl-L-arginyl-L-lysyl-L-lysyl-L-arginyl-L-arginyl-L-glutamyl-L-arginyl-L-arginyl-L-arginyl- (CA INDEX NAME)



RN 418763-88-9 CAPLUS

CN L-Proline, L-leucyl-L-lysyl-L-leucyl-L-α-glutamyl-L-prolyl-L-asparaginyl- (9CI) (CA INDEX NAME)

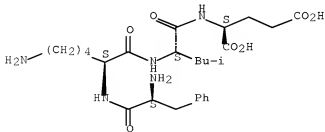
Absolute stereochemistry.



RN 418763-89-0 CAPLUS

CN L-Glutamic acid, L-phenylalanyl-L-lysyl-L-leucyl- (9CI) (CA INDEX NAME)

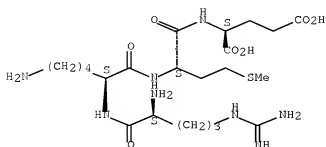
Absolute stereochemistry.



RN 418763-90-3 CAPLUS

CN L-Glutamic acid, L-arginyl-L-lysyl-L-methionyl- (9CI) (CA INDEX NAME)

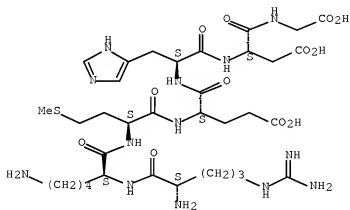
Absolute stereochemistry.



RN 418763-91-4 CAPLUS

CN Glycine, L-arginyl-L-lysyl-L-methionyl-L- α -glutamyl-L-histidyl-L- α -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

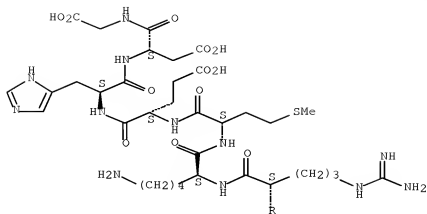


RN 418763-93-6 CAPLUS

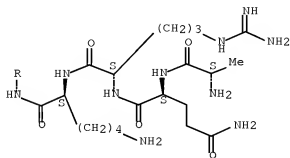
CN Glycine, L-alanyl-L-glutaminyl-L-arginyl-L-lysyl-L-arginyl-L-lysyl-L-methionyl-L- α -glutamyl-L-histidyl-L- α -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

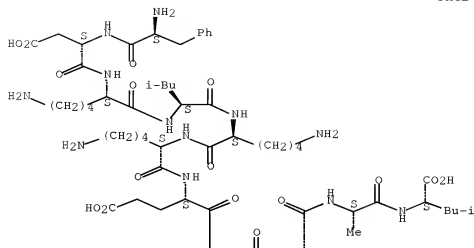


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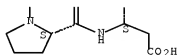
CN L-Leucine, L-phenylalanyl-L- α -aspartyl-L-lysyl-L-leucyl-L-lysyl-L-lysyl-L- α -glutamyl-L-prolyl-L- α -aspartyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

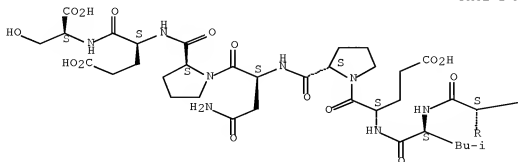


RN 418763-95-8 CAPLUS

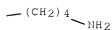
CN L-Serine, L- α -glutamyl-L-valyl-L-alanyl-L-leucyl-L-lysyl-L-leucyl-L- α -glutamyl-L-prolyl-L-asparaginyl-L-prolyl-L- α -glutamyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

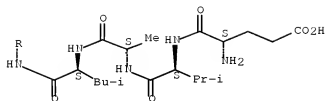
PAGE 1-A



PAGE 1-B



PAGE 2-A

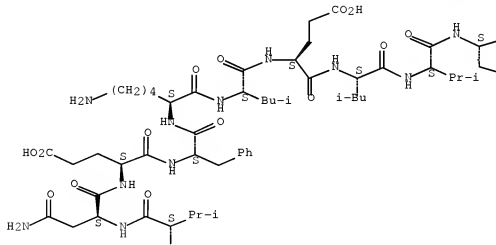


RN 418763-96-9 CAPLUS

CN L-Glutamic acid, L- α -aspartyl-L-methionyl-L-valyl-L-asparaginyl-L- α -glutamyl-L-phenylalanyl-L-lysyl-L-leucyl-L- α -glutamyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

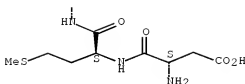
PAGE 1-A



PAGE 1-B



PAGE 2-A



IT 418763-86-7

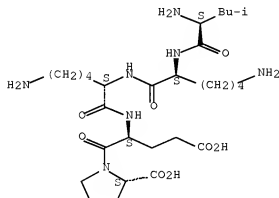
RL: PRP (Properties)

(unclaimed sequence; compns. and methods for treating hematol. malignancies and multiple drug resistance by modulating mdrl gene and inhibit hypoxia inducible factor-1 gene expression)

RN 418763-86-7 CAPLUS

CN L-Proline, L-leucyl-L-lysyl-L-lysyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 21 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:808254 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 135:362538

TITLE:

INVENTOR(S): Baserga, Renato; Abraham, David; Resnicoff, Mariana

PATENT ASSIGNEE(S): Thomas Jefferson University, USA

SOURCE: U.S., 35 pp., Cont.-in-part of U.S. 5,714,170.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6312684	B1	20011106	US 1997-864641	19970529 <--
WO 9614746	A1	19960523	WO 1995-US14952	19951115 <--
W: CA, JP, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6541036	B1	20030401	US 1999-374712	19990813 <--
US 20010022977	A1	20010920	US 2001-832382	20010411 <--
US 6506415	B2	20030114		

PRIORITY APPLN. INFO.:

US 1994-340732	A2	19941116 <--
WO 1995-US14952	A2	19951115 <--
US 1997-864641	A1	19970529 <--
US 1998-96354P	P	19980813 <--
US 1998-113599P	P	19981224 <--

AB A method of inducing resistance to tumor growth comprising placing tumor cells in culture in vitro supplemented with a pro-apoptotic agent for a period of time, transferring the tumor cells into a diffusion chamber, thereby producing a cell-containing chamber, inserting the chamber into a mammal for a therapeutically effective time, thereby inducing resistance to tumor growth. The pro-apoptotic agents include nucleic acid mols., proteins or peptides, non-proteins or non-polynucleotide compds., and a phys. conditions.

IC ICM A61K048-00
 ICS A61K035-00

INCL 424093210

CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1, 15

IT Neoplasm
 (MHC class I stimulation of; diffusion chamber containing tumor cell culture for inducing resistance to tumor growth)

IT Intestine, neoplasm
 (colon; diffusion chamber containing tumor cell culture for inducing resistance to tumor growth)

IT Animal tissue culture
 Antitumor agents
 Apoptosis
 Cell death
 Drug screening
 Genetic vectors
 Lung, neoplasm
 Melanoma
 Molecular cloning
 Ovary, neoplasm
 Pancreas, neoplasm
 Protein sequences
 cDNA sequences
 (diffusion chamber containing tumor cell culture for inducing resistance to tumor growth)

IT Antitumor agents
 (vaccines; diffusion chamber containing tumor cell culture for inducing resistance to tumor growth)

IT 156761-76-1 162558-12-5 197926-41-3
 200875-64-5 200875-75-8 204442-95-5
 204443-05-0 259202-42-1 259242-70-1, 3: PN: WO0009145 SEQID: 4
 unclaimed DNA 259242-71-2, 4: PN: WO0009145 SEQID: 5 unclaimed DNA
 259242-72-3, 5: PN: WO0009145 SEQID: 6 unclaimed DNA 259242-73-4, 6: PN:
 WO0009145 SEQID: 7 unclaimed DNA 259242-74-5, 7: PN: WO0009145 SEQID: 8

unclaimed DNA 371972-51-9

RL: PEP (Physical, engineering or chemical process); PRP (Properties);
THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)

(diffusion chamber containing tumor cell culture for inducing
resistance to tumor growth)

IT 156761-76-1 162558-12-5 200875-64-5
200875-75-3 204442-95-5 204443-05-6
371972-51-9

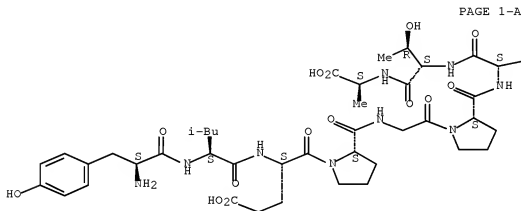
RL: PEP (Physical, engineering or chemical process); PRP (Properties);
THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)

(diffusion chamber containing tumor cell culture for inducing
resistance to tumor growth)

RN 156761-76-1 CAPLUS

CN L-Alanine, L-tyrosyl-L-leucyl-L- α -glutamyl-L-prolylglycyl-L-prolyl-L-
valyl-L-threonyl- (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

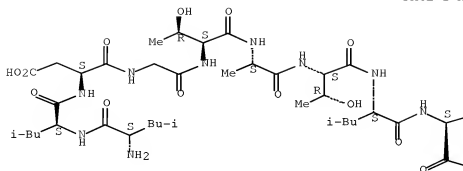
Pr-i

RN 162558-12-5 CAPLUS

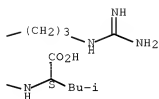
CN L-Leucine, L-leucyl-L-leucyl-L- α -aspartylglycyl-L-threonyl-L-alanyl-
L-threonyl-L-leucyl-L-arginyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

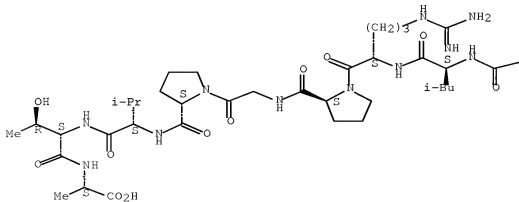


RN 200875-64-5 CAPLUS

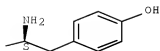
CN L-Alanine, L-tyrosyl-L-leucyl-L-arginyl-L-prolylglycyl-L-prolyl-L-valyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

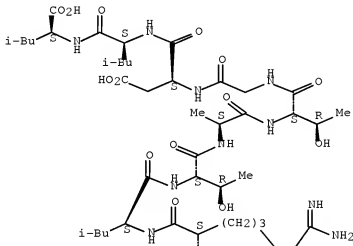


RN 200875-75-8 CAPLUS

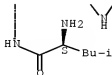
CN L-Leucine, L-leucyl-L-arginyl-L-leucyl-L-threonyl-L-alanyl-L-threonylglycyl-L- α -aspartyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



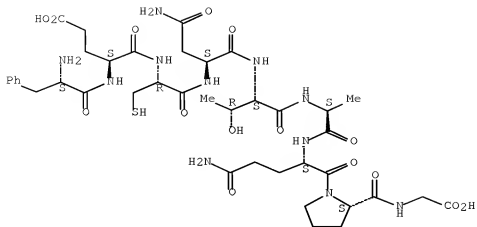
PAGE 2-A



RN 204442-95-5 CAPLUS

CN Glycine, L-phenylalanyl-L- α -glutamyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-glutaminy-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

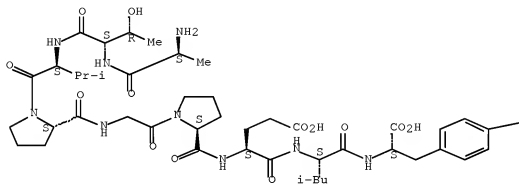


RN 204443-05-0 CAPLUS

CN L-Tyrosine, L-alanyl-L-threonyl-L-valyl-L-prolylglycyl-L-prolyl-L- α -glutamyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B

—OH

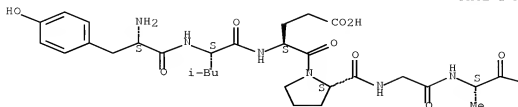
RN 371972-51-9 CAPLUS

CN L-Alanine, L-tyrosyl-L-leucyl-L- α -glutamyl-L-prolylglycyl-L-alanyl-L-

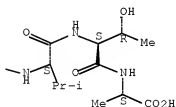
valyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

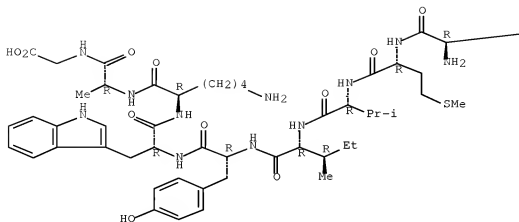
L80 ANSWER 22 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2001:661456 CAPLUS Full-text
 DOCUMENT NUMBER: 135:221277
 TITLE: Peptides and methods for modulating cell adhesion-mediated drug resistance
 INVENTOR(S): Dalton, William S.; Damiano, Jason S.; Cress, Anne E.
 PATENT ASSIGNEE(S): University of South Florida, USA
 SOURCE: PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064714	A2	20010907	WO 2001-US6397	20010301 <--
WO 2001064714	A3	20020328		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-186198P	P 20000301 <--

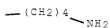
- AB The invention discloses peptides and methods of their use for inhibiting drug- and radiation-therapy resistance in cancerous cells, in which efficacy of chemotherapy and/or radiotherapy of a patient is enhanced by administration of an effective amount of a peptide that inhibits cell adhesion-mediated drug resistance (CAM-DR). Preferably, the peptide comprises D-amino acids having the sequence: kmviywkag (RZ-3), or is a variant or modified version thereof. The peptide is preferably administered to the patient prior to chemotherapy and/or radiation therapy. Inhibition of CAM-DR by RZ-3 in multiple myeloma cells is disclosed.
- IC ICM C07K007-00
- CC 1-6 (Pharmacology)
- IT Antitumor agents
(multiple myeloma; peptides and methods for modulating cell adhesion-mediated drug resistance)
- IT Antitumor agents
(myeloma; peptides and methods for modulating cell adhesion-mediated drug resistance)
- IT Antitumor agents
Apoptosis
Cell adhesion
Chemotherapy
Drug delivery systems
Drug interactions
Drug resistance
Gamma ray
Radiotherapy
(peptides and methods for modulating cell adhesion-mediated drug resistance)
- IT 351327-12-3 351327-12-3D, variants
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides and methods for modulating cell adhesion-mediated drug resistance)
- IT 57-21-7, Vincristine 147-94-4, Ara-C 148-82-3, Melphalan 23214-92-8, Doxorubicin 65271-80-9, Mitoxantrone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides and methods for modulating cell adhesion-mediated drug resistance)
- IT 351327-12-3 351327-12-3U, variants
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides and methods for modulating cell adhesion-mediated drug resistance)
- RN 351327-12-3 CAPLUS
- CN Glycine, D-lysyl-D-methionyl-D-valyl-D-isoleucyl-D-tyrosyl-D-tryptophyl-D-lysyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

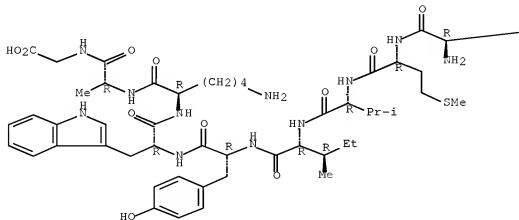


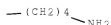
RN 351327-12-3 CAPLUS

CN Glycine, D-lysyl-D-methionyl-D-valyl-D-isoleucyl-D-tyrosyl-D-tryptophyl-D-lysyl-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





IT 57-22-7, Vincristine

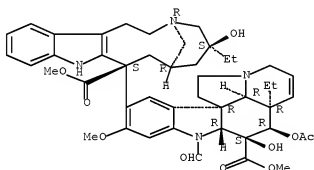
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides and methods for modulating cell adhesion-mediated drug resistance)

RN 57-22-7 CAPLUS

CN Vincalukoblastine, 22-oxo- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L80 ANSWER 23 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:636361 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 135:205530

TITLE: Compositions and methods of use of HET, a novel modulator of estrogen action

INVENTOR(S): Oesterreich, Steffi; Osborne, C. K.; Lee, A. V.; Fuqua, S. A.

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001063292	A2	20010830	WO 2001-US6135	20010222 <--
WO 2001063292	A3	20020328		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,			

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-184097P P 20000222 <--

AB Disclosed are methods for the detection of tumor cells, in particular human breast cancer cells. Genetic and antibody probes and methods useful in determining the presence of and monitoring tumor cell proliferation are also described. The methods involve determining HET polypeptide expression, mRNA levels or loss of heterozygosity at human chromosomal locus 19p13 as a measure of tumor cell malignancy. These methods are also of use in distinguishing breast cancers that are resistant to estrogen antagonists, such as tamoxifen, from estrogen antagonist sensitive tumors. Also described are procedures for transforming cells with HET gene containing vectors that express HET polypeptide. Such procedures may be of use in converting tamoxifen-resistant tumors into tamoxifen-sensitive tumors.

IC ICM G01N033-574

CC 1-6 (Pharmacology)

Section cross-reference(s): 3, 9, 14

IT Antitumor agents
 (mammary gland carcinoma; compns. and methods of use of novel modulator of estrogen action HET for the diagnosis and treatment of breast cancer in relation to resistance to antiestrogens)

IT Antitumor agents
 (mammary gland; compns. and methods of use of novel modulator of estrogen action HET for the diagnosis and treatment of breast cancer in relation to resistance to antiestrogens)

IT Antitumor agents
 (resistance to; compns. and methods of use of novel modulator of estrogen action HET for the diagnosis and treatment of breast cancer in relation to resistance to antiestrogens)

IT 226885-80-9
 RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (anti-HET/SAF-B monoclonal antibodies generation by; compns. and methods of use of novel modulator of estrogen action HET for the diagnosis and treatment of breast cancer in relation to resistance to antiestrogens)

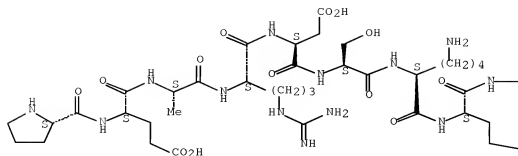
IT 226885-80-9
 RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (anti-HET/SAF-B monoclonal antibodies generation by; compns. and methods of use of novel modulator of estrogen action HET for the diagnosis and treatment of breast cancer in relation to resistance to antiestrogens)

RN 226885-80-9 CAPLUS

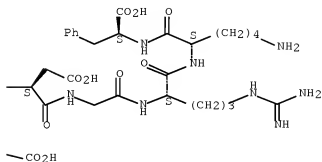
CN L-Phenylalanine, L-prolyl-L- α -glutamyl-L-alanyl-L-arginyl-L- α -aspartyl-L-seryl-L-lysyl-L- α -glutamyl-L- α -aspartylglycyl-L-arginyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 24 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:487157 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:226380

TITLE: Treatment with inhibitors of caspases, that are substrates of drug transporters, selectively permits chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells

AUTHOR(S): Blagosklonny, M. V.

CORPORATE SOURCE: Medicine Branch, National Cancer Institute, NIH, Bethesda, MD, 20892, USA

SOURCE: Leukemia (2001), 15(6), 936-941

CODEN: LEUKED; ISSN: 0887-6924

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Many chemotherapeutic agents induce apoptosis in tumor cells, but killing of normal cells remains a major obstacle. Development of multidrug resistance further limits chemotherapy in cancer. Here, I show that multidrug resistance can be exploited for selective killing of multidrug-resistant cells by a combination of an apoptosis-inducing agent that is not a substrate of either Pgp or MRP (eg flavopiridol) with a caspase inhibitor that is a substrate (eg Z-DEVD-fmk). In normal cells, treatment with caspase inhibitors prevented PARP cleavage, nuclear fragmentation, and cell death caused by flavopiridol or epothilone B. In contrast, Pgp- and MRP-expressing cells were not rescued by

caspase inhibitors. Furthermore, reversal of drug resistance renders Pgp cells sensitive to caspase inhibitors abolishing therapeutic advantage. Thus, caspase inhibitors, that are inactive in multidrug-resistant cells, protect normal but not multidrug-resistant cells against chemotherapy, permitting selective eradication of multidrug-resistant cells. Clin. application of this approach may diminish the toxic side-effects of chemotherapy in patients with multidrug-resistant tumors.

CC 1-6 (Pharmacology)

IT Antitumor agents

(leukemia; caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

IT Antitumor agents

(resistance to; caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

IT 146426-40-6, Flavopiridol 152044-54-7, Epothilone B 210344-95-9

220644-02-0 220760-26-9 220760-27-0

220760-28-1 325766-54-7 403601-94-5

RL: PAC (Pharmacological activity); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)

(caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

IT 210344-95-9 220644-02-0 220760-26-9

220760-27-0 220760-28-1 325766-54-7

403601-94-5

RL: PAC (Pharmacological activity); THU (Therapeutic

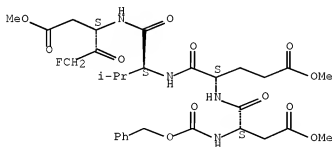
use); BIOL (Biological study); USES (Uses)

(caspase inhibitors (drug transporters substrates) selectively permit chemotherapy-induced apoptosis in multidrug-resistant cells but protects normal cells)

RN 210344-95-9 CAPLUS

CN L-Valinamide, N-[(phenylmethoxy)carbonyl]-L- α -aspartyl-L- α -glutamyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, 1,2-dimethyl ester (CA INDEX NAME)

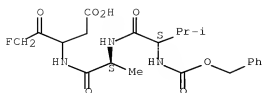
Absolute stereochemistry.



RN 220644-02-0 CAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (CA INDEX NAME)

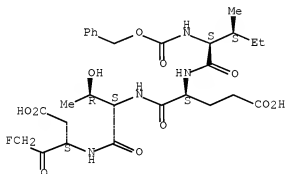
Absolute stereochemistry.



RN 220760-26-9 CAPLUS

CN L-Threoninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L- α -glutamyl-N-[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (CA INDEX NAME)

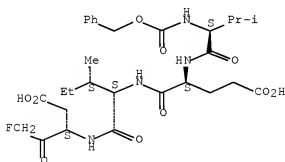
Absolute stereochemistry.



RN 220760-27-0 CAPLUS

CN L-Isoleucinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-L- α -glutamyl-N-[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (CA INDEX NAME)

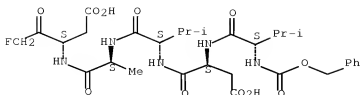
Absolute stereochemistry.



RN 220760-28-1 CAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-valyl-L- α -aspartyl-L-valyl-N-[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

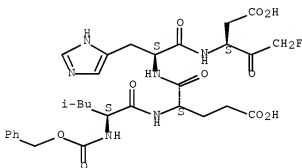
Absolute stereochemistry.



RN 325786-54-7 CAPLUS

CN L-Histidinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-L- α -glutamyl-N-[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (CA INDEX NAME)

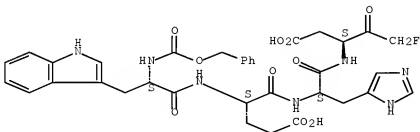
Absolute stereochemistry.



RN 403601-94-5 CAPLUS

CN L-Histidinamide, N-[(phenylmethoxy)carbonyl]-L-tryptophyl-L- α -glutamyl-N-[(1S)-1-(carboxymethyl)-3-fluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 25 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:400655 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 135:235892

TITLE: Effects of chemically modified tetracyclines (CMTs) in sensitive, multidrug resistant and apoptosis resistant leukemia cell lines

AUTHOR(S): Tolomeo, Manlio; Grimaudo, Stefania; Milano, Salvatore; La Rosa, Marzia; Ferlazzo, Viviana; Di Bella, Gloria; Barbera, Caterina; Simoni, Daniele; D'Agostino, Pietro; Cillari, Enrico

CORPORATE SOURCE: Divisione di Ematologia e Servizio AIDS, Policlinico Universitario Paolo Giaccone, Palermo, 90127, Italy

SOURCE: British Journal of Pharmacology (2001), 133(2), 306-314
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recently discovered chemical modified tetracyclines (CMTs) have shown in vitro and in vivo anti-proliferative and anti-tumor activities. Here, we evaluated in vitro the anti-proliferative and apoptotic activity of six different dedimethylamino chemical modified tetracyclines (CMT-1, CMT-3, CMT-5, CMT-6, CMT-7 and CMT-8) in sensitive and multidrug resistant myeloid leukemia cells (HL60 and HL60R) in vitro. Three of these compds. (CMT-5, CMT-6, CMT-7) showed low cytotoxic activity both in sensitive and in resistant cells, CMT-3 was endowed with a high anti-proliferative activity only in sensitive cells and was moderately effective as apoptosis inducing agent, with an activity similar to that shown by doxycycline. On the contrary, CMT-1 and CMT-8 were very effective as programmed cell death inducing agents. FasThe apoptotic pathway activated by these compds. involved the activation of caspases, especially caspase-9 and, for CMT-1, also the activation of Fas. Interestingly CMT-8, but not CMT-1, was able to induce apoptosis in multidrug resistant HL60R and in Fas-ligand resistant HUT78B1 cell lines. These properties, together with others previously described (e.g. anti-metastatic and anti-osteolytic activities), suggest that CMT-8 may have important applications in the clin. management of cancer. The comparative anal. of structure-activity relationship of CMT-8 and doxycycline suggests that the C-5 hydroxy moiety may play an important role in conferring activity in multidrug resistant cells. These findings appear to support the hypothesis that CMT-8 may represent an interesting lead for the development of a new class of potent apoptosis inducer agents active in multidrug resistant and Fas-ligand resistant malignancies.

CC 1-3 (Pharmacology)

IT Antitumor agents
(metastasis; chemical modified tetracyclines SAR in sensitive, multidrug resistant and apoptosis resistant leukemia cell lines)

IT Antitumor agents
(resistance to; chemical modified tetracyclines SAR in sensitive, multidrug resistant and apoptosis resistant leukemia cell lines)

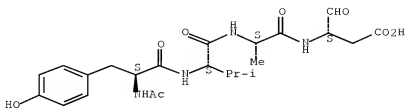
IT 143313-51-3 169332-60-9, DEVD-CHO 187389-52-2, ZVAD-fmk 359865-35-3
RL: EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(chemical modified tetracyclines SAR in sensitive, multidrug resistant and apoptosis resistant leukemia cell lines)

IT 143313-51-3 169332-60-9, DEVD-CHO 187389-52-2, ZVAD-fmk 359865-35-3
RL: EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(chemical modified tetracyclines SAR in sensitive, multidrug resistant and apoptosis resistant leukemia cell lines)

RN 143313-51-3 CAPLUS

CN L-Alaninamide, N-acetyl-L-tyrosyl-L-valyl-N-[(1S)-2-carboxy-1-formylethyl]-
(CA INDEX NAME)

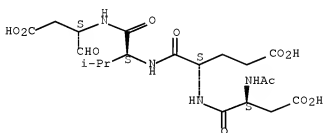
Absolute stereochemistry.



RN 169332-60-9 CAPLUS

CN L-Valinamide, N-acetyl-L- α -aspartyl-L- α -glutamyl-N-[(1S)-2-carboxy-1-formylethyl]- (CA INDEX NAME)

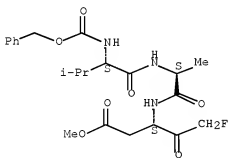
Absolute stereochemistry.



RN 187389-52-2 CAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[(1S)-3-fluoro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]- (CA INDEX NAME)

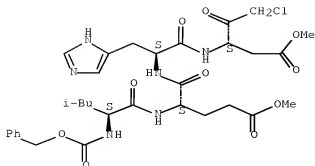
Absolute stereochemistry.



RN 359865-35-3 CAPLUS

CN L-Histidinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-L- α -glutamyl-N-[(1S)-3-chloro-1-(2-methoxy-2-oxoethyl)-2-oxopropyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 26 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:26870 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 135:132865

TITLE: Dominant effector genetics in mammalian cells

AUTHOR(S): Xu, Xiang; Leo, Cindy; Jang, Yngju; Chan, Eva; Padilla, David; Huang, Betty C. B.; Lin, Tong; Gururaja, Tarikere; Hitoshi, Yasumichi; Lorens, James B.; Anderson, David C.; Sikic, Branimir; Luo, Ying; Payan, Donald G.; Nolan, Garry P.

CORPORATE SOURCE: Department of Molecular Pharmacology, Department of Microbiology and Immunology, Stanford University, Palo Alto, CA, USA

SOURCE: Nature Genetics (2001), 27(1), 23-29

CODEN: NGENEC; ISSN: 1061-4036

PUBLISHER: Nature America Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have expressed libraries of peptides in mammalian cells to select for trans-dominant effects on intracellular signaling systems. As an example-and to reveal pharmacol. relevant points in pathways that lead to Taxol resistance-the authors selected for peptide motifs that confer resistance to Taxol-induced cell death. Of several peptides selected, one, termed RGP8.5, was linked to upregulation of expression of the gene ABCB1 (also known as MDR1, for multiple drug resistance) in HeLa cells. Our data indicate that trans-dominant effector peptides can point to potential mechanisms by which signaling systems operate. Such tools may be useful in functional genomic anal. of signaling pathways in mammalian disease processes.

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 1

IT Antitumor agents

(mammary gland; intracellular expression of random peptide libraries in mammalian cells, selection of peptides conferring taxol resistance, identification of gene ABCB1/MDR1 upregulation by RGP8.5 peptide, and RGP8.5 association with proteasome)

IT 299170-91-5 310871-14-8 351325-39-9 351435-75-1

351435-80-8 351435-90-0 351435-91-1

RL: BAC (Biological activity or effector, except adverse); BSU

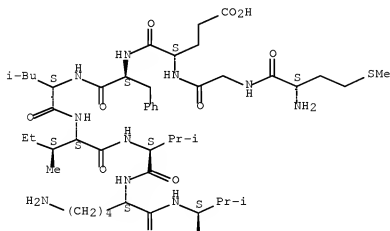
(Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(intracellular expression of random peptide libraries in mammalian cells, selection of peptides conferring taxol resistance, identification of gene ABCB1/MDR1 upregulation by RGP8.5 peptide, and

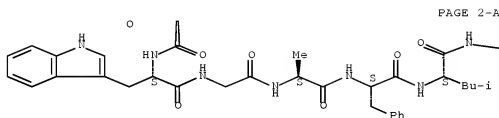
- RGP8.5 association with proteasome)
- IT 33969-62-4, Taxol
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (intracellular expression of random peptide libraries in mammalian cells, selection of peptides conferring taxol resistance, identification of gene ABCB1/MDR1 upregulation by RGP8.5 peptide, and RGP8.5 association with proteasome)
- IT 351325-39-8
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (intracellular expression of random peptide libraries in mammalian cells, selection of peptides conferring taxol resistance, identification of gene ABCB1/MDR1 upregulation by RGP8.5 peptide, and RGP8.5 association with proteasome)
- RN 351325-39-8 CAPLUS
- CN Glycine, L-methionylglycyl-L- α -glutamyl-L-phenylalanyl-L-leucyl-L-isoleucyl-L-valyl-L-lysyl-L-valyl-L-tryptophylglycyl-L-alanyl-L-phenylalanyl-L-leucyl-L-valyl-L-seryl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

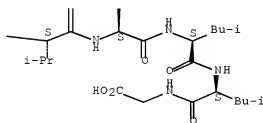
PAGE 1-A



PAGE 1-B



PAGE 2-B



IT 33069-62-4, Taxol

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

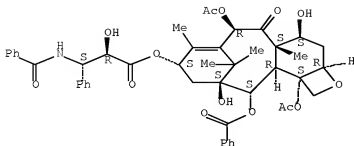
(intracellular expression of random peptide libraries in mammalian cells, selection of peptides conferring taxol resistance, identification of gene ABCB1/MDR1 upregulation by RGP8.5 peptide, and RGP8.5 association with proteasome)

RN 33069-62-4 CAPLUS

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (α R, β S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 27 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:911119 CAPLUS Full-text
 DOCUMENT NUMBER: 134:66133
 TITLE: Chemotherapeutic agent-peptide compositions for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compositions
 INVENTOR(S): Tuszyński, George; Williams, Taffy; Actor, Paul
 PATENT ASSIGNEE(S): USA
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078359	A2	20001228	WO 2000-US16955	20000621 <--
WO 2000078359	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-140310P P 19990621 <--

AB The invention provides methods and compns. for treating cancer and chemotherapy-resistant cancers comprising a chemotherapeutic agent conjugated to or co-administered with a peptide.

IC ICM A61K047-48

CC 1-6 (Pharmacology)

Section cross-reference(s): 63

IT Antitumor agents

(and peptide conjugates; chemotherapeutic agent-peptide compns. for

- treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Lung, neoplasms
Mammary gland
(carcinoma, inhibitors; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Antitumor agents
(lung carcinoma; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Antitumor agents
(lung, metastasis, from melanoma; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Antitumor agents
(mammary gland carcinoma; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Antitumor agents
(melanoma, metastasis, to lung; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Antitumor agents
(melanoma; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT Lung, neoplasms
(metastasis, inhibitors, from melanoma; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 138849-27-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT 313950-23-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT 23214-92-8D, Doxorubicin, peptide conjugates 33069-62-4D, Paclitaxel, peptide conjugates 138849-27-1D, chemotherapeutic conjugates 142116-67-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT 131204-46-1 138849-24-8 142116-64-1 152606-70-7
RL: PRP (Properties)
(unclaimed protein sequence; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)
- IT 315179-75-0 315179-76-1
RL: PRP (Properties)

(unclaimed sequence; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)

IT 33069-62-4, Paclitaxel 138849-27-1

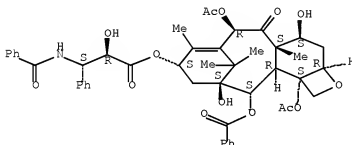
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)

RN 33069-62-4 CAPLUS

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (α R, β S)- (CA INDEX NAME)

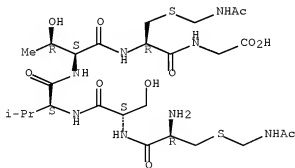
Absolute stereochemistry. Rotation (-).



RN 138849-27-1 CAPLUS

CN Glycine, S-[(acetylamino)methyl]-L-cysteinyl-L-seryl-L-valyl-L-threonyl-S-[(acetylamino)methyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 313950-23-1F

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(chemotherapeutic agent-peptide compns. for treating chemotherapy-

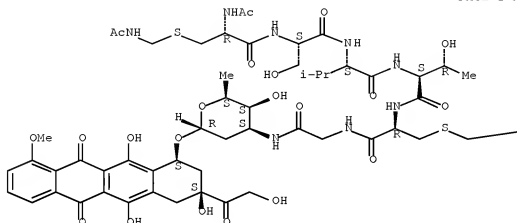
resistant tumor cells, and targeted chemotherapy compns.)

RN 313950-23-1 CAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[N-acetyl-S-[(acetylamino)methyl]-L-cysteinyl-L-seryl-L-valyl-L-threonyl-S-[(acetylamino)methyl]-L-cysteinylglycyl]amino]-2,3,6-trideoxy- α -L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—NHAc

IT 33069-62-4D, Paclitaxel, peptide conjugates 138849-27-1D, chemotherapeutic conjugates 142116-67-4

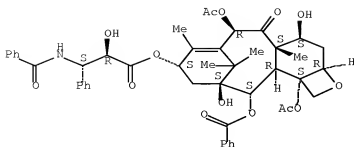
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)

RN 33069-62-4 CAPLUS

CN Benzenepropanoic acid, β -(benzoylamino)- α -hydroxy-, (2aR, 4S, 4aS, 6R, 9S, 11S, 12S, 12aR, 12bS)-6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca[3, 4]benz[1, 2-b]oxet-9-yl ester, (α R, β S)- (CA INDEX NAME)

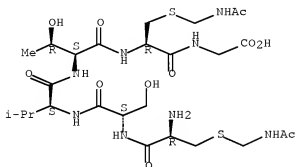
Absolute stereochemistry. Rotation (-).



RN 138849-27-1 CAPLUS

CN Glycine, S-[(acetylamino)methyl]-L-cysteinyl-L-seryl-L-valyl-L-threonyl-S-[(acetylamino)methyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

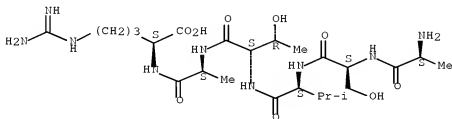
Absolute stereochemistry.



RN 142116-67-4 CAPLUS

CN L-Arginine, L-alanyl-L-seryl-L-valyl-L-threonyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 131204-46-1 138849-24-8 142116-64-1
152606-70-7

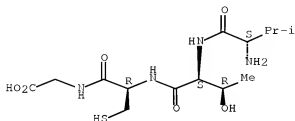
RL: PRP (Properties)

(unclaimed protein sequence; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)

RN 131204-46-1 CAPLUS

CN Glycine, L-valyl-L-threonyl-L-cysteinyl- (CA INDEX NAME)

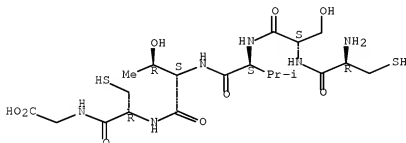
Absolute stereochemistry.



RN 138849-24-8 CAPLUS

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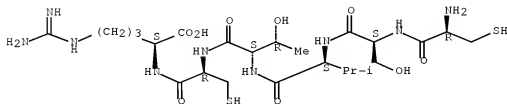
Absolute stereochemistry.



RN 142116-64-1 CAPLUS

CN L-Arginine, L-cysteinyl-L-seryl-L-valyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)

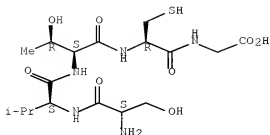
Absolute stereochemistry.



RN 152606-70-7 CAPLUS

CN Glycine, L-seryl-L-valyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 315179-75-0 315179-76-1

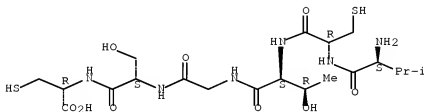
RL: PRP (Properties)

(unclaimed sequence; chemotherapeutic agent-peptide compns. for treating chemotherapy-resistant tumor cells, and targeted chemotherapy compns.)

RN 315179-75-0 CAPLUS

CN L-Cysteine, L-valyl-L-cysteinyl-L-threonylglycyl-L-seryl- (9CI) (CA INDEX NAME)

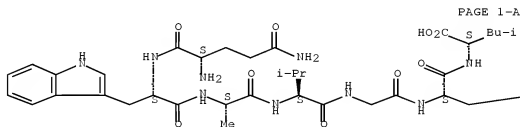
Absolute stereochemistry.



RN 315179-76-1 CAPLUS

CN L-Leucine, L-glutamyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl- (CA INDEX NAME)

Absolute stereochemistry.





L80 ANSWER 28 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:880923 CAPLUS Full-text
 DOCUMENT NUMBER: 134:37055
 TITLE: Methods and compositions using FGF inhibitors and agonists for modulating cell proliferation and cell death
 INVENTOR(S): Au, Jessie L. S.; Wientjes, M. Guillaume
 PATENT ASSIGNEE(S): USA
 SOURCE: PCT Int. Appl., 143 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074634	A2	20001214	WO 2000-US40103	20000605 <--
WO 2000074634	A3	20010823		
WO 2000074634	A9	20020926		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377385	A1	20001214	CA 2000-2377385	20000605 <--
EP 1206234	A2	20020522	EP 2000-943429	20000605 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003503313	T	20030128	JP 2001-501171	20000605 <--
US 6599912	B1	20030729	US 2000-587559	20000605 <--
AU 780454	B2	20050324	AU 2000-57903	20000605 <--
US 20040010001	A1	20040115	US 2003-464018	20030618 <--
PRIORITY APPLN. INFO.:				
			US 1999-137345P	P 19990603 <--
			US 1999-165983P	P 19991117 <--
			US 1999-172031P	P 19991223 <--
			US 2000-187445P	P 20000307 <--
			US 2000-587559	A3 20000605 <--
			WO 2000-US40103	W 20000605 <--
AB	Methods and comps. for modulating the FGF effect on the sensitivity of malignant and normal cells to anticancer agents are provided. In particular, methods and comps. for inhibiting FGF-induced resistance to a broad spectrum			

of anticancer agents in solid and soft-tissue tumors, metastatic lesions, leukemia and lymphoma are provided. Preferably, the compns. include at least one FGF inhibitor in combination with a cytotoxic agents, e.g., antimicrotubule agents, topoisomerase I inhibitors, topoisomerase II inhibitors, antimetabolites, mitotic inhibitors, alkylating agents, intercalating agents, agents capable of interfering with a signal transduction pathway (e.g., g., a protein kinase C inhibitor, e.g., an anti-hormone, e.g., an antibody against growth factor receptors), an agent that promote apoptosis and/or necrosis, an interferon, an interleukin, a tumor necrosis factor, and radiation. In other embodiments, methods and composition for protecting a cell in a subject, from one or more of killing, inhibition of growth or division or other damage caused, e.g., by a cytotoxic agent, are provided. Preferably, the method includes administering to the subject an effective amount of at least one FGF agonist, thereby treating the cell, e.g., protecting or reducing the damage to the dividing cell from said cytotoxic agent. FGF gene expression-based methods for diagnosis of proliferative disorders are also disclosed.

- ICI A61
- CC 1-12 (Pharmacology)
- Section cross-reference(s): 2
- ST FGF inhibitor agonist antitumor cytoprotectant; resistance
- antitumor agent FGF inhibitor; proliferative disorder diagnosis FGF gene
- IT Antitumor agents
 - (Ewing's sarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Alkylating agents, biological
 - Antitumor agents
 - Apoptosis
 - Cirrhosis
 - Cyst, pathological
 - Cytotoxic agents
 - Drug delivery systems
 - Drug resistance
 - Necrosis
 - Psoriasis
 - Radiotherapy
 - (FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
 - (Kaposi's sarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
 - (Wilms' tumor; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Kidney, neoplasm
 - (Wilms', inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Nerve, neoplasm
 - (acoustic neuroma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
 - (acoustic neuroma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
 - (adenocarcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Intestine, neoplasm
 - (adenoma, small intestine; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Liver, neoplasm

Stomach, neoplasm
 (adenoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Microtubule
 (anti-microtubule agents; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (astrocytoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (bile duct carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (bladder carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (brain; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (bronchi carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Bladder
 Bronchi

Lung, neoplasm

Sebaceous gland
 (carcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Uterus, neoplasm
 (cervix, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (cervix; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (chondroblastoma; GF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (chondrosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (chordoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (choriocarcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
 (colon carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Intestine, neoplasm
 (colon, adenoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Intestine, neoplasm
 (colon, carcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Intestine, neoplasm
 (colon, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)

- IT Intestine, neoplasm
(colon, polyp; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(colon; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(craniopharyngioma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Ovary, neoplasm
(cystadenocarcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(cystadenocarcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Neoplasm
(diagnosis; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(enchondroma; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Brain, neoplasm
(ependymoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(ependymoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Genetics
(epigenetics, epigenetic mechanism of antitumor drug resistance ; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Neoplasm
(epithelioma, adenomyoepithelioma, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(esophagus; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Neoplasm
(fibroma, chondromyxoid fibroma inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(fibrosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(glioma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Neoplasm
(hamartoma, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(head; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Blood vessel, neoplasm
(hemangioblastoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Blood vessel, neoplasm
(hemangioma, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(hemangioma; GF inhibitors and agonists for modulating cell

- proliferation and cell death)
- IT Blood vessel, neoplasm
(hemangiosarcoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(hemangiosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Liver, neoplasm
(hepatoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(hepatoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Adenoma
- Brain, neoplasm
- Ovary, neoplasm
- Pancreas, neoplasm
- Papilloma
- Skin, neoplasm
- Stomach, neoplasm
- Testis, neoplasm
- Uterus, neoplasm
(inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(leiomyoma inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(leiomyosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(leukemia; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Adipose tissue, neoplasm
(lipoma, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lipoma; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Adipose tissue, neoplasm
(liposarcoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(liposarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lung carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lung non-small-cell carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lung small-cell carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lymphangiosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(lymphoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

- IT Antitumor agents
(mammary gland; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Brain, neoplasm
(medulloblastoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(medulloblastoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(melanoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(meningioma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(mesothelioma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(metastasis; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(myosarcoma inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(neck; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Nerve, neoplasm
(neuroblastoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(neuroblastoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Lung, neoplasm
(non-small-cell carcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(oligodendroglioma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Kidney, neoplasm
(oncocyoma and papilloma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(oncocyoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(osteoblastoma; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(osteochondroma; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(osteoid osteoma; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Bone, neoplasm
(osteoid, osteoma, inhibitors; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(osteoma; GF inhibitors and agonists for modulating cell proliferation and cell death)

- IT Bone, neoplasm
(osteosarcoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(ovary; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(pancreas; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(papilloma inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(pinealoma inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(prostate gland, metastasis; GF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(prostate gland; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Intestine, neoplasm
(rectum, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(rectum; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Kidney, neoplasm
(renal cell carcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(renal cell carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Eye, neoplasm
(retinoblastoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(retinoblastoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(rhabdomyosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(sarcoma, lymphangi endotheliosarcoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(schwannoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(sebaceous gland carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Testis, neoplasm
(seminoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(seminoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)
- IT Antitumor agents
(skin; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Lung, neoplasm
(small-cell carcinoma, inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(squamous cell carcinoma; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(stomach; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(synovial membrane tumor inhibitors; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(testis; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(uterus; FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(vaccines; GF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(vaginal tumor inhibitors, papilloma; GF inhibitors and agonists for modulating cell proliferation and cell death)

IT Antitumor agents
(vulva papilloma, polyp and papilloma; GF inhibitors and agonists for modulating cell proliferation and cell death)

IT 51-21-8, 5-Fluorouracil 145-63-1, Suramin 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate 10540-29-1, Tamoxifen 13311-84-7, Flutamide 15663-27-1, Cisplatin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 53714-56-0, Leuprolide 56420-45-2, Epirubicin 62031-54-3D, Fibroblast growth factor, fragments 65277-42-1, Ketoconazole 65807-02-5, Goserelin 74578-38-4, UFT 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 106096-92-8D, Acidic fibroblast growth factor, fragments and analogs 106096-93-9D, Basic fibroblast growth factor, fragments and analogs 114977-28-5, Taxotere

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FGF inhibitors and agonists for modulating cell proliferation and cell death)

IT 53714-56-0, Leuprolide 65807-02-5, Goserelin

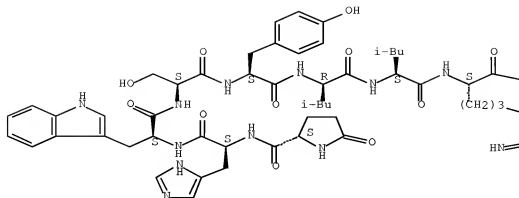
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FGF inhibitors and agonists for modulating cell proliferation and cell death)

RN 53714-56-0 CAPLUS

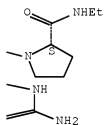
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

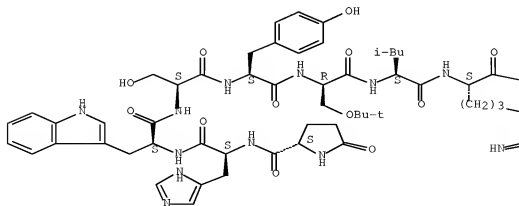


RN 65807-02-5 CAPLUS

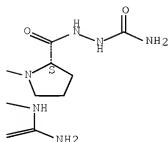
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 29 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:475504 CAPLUS Full-text
 DOCUMENT NUMBER: 133:118947
 TITLE: Method and means for reducing chemotherapeutic drug resistance in-situ within neoplasms of epithelial cell origin
 INVENTOR(S): Kocher, Olivier N.
 PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Inc., USA
 SOURCE: PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040201	A2	20000713	WO 1999-US30876	19991222 <--
WO 2000040201	A3	20000921		

W: AU, CA, JP
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-224623 A 19981231 <--

AB The present invention provides a method and composition means for reducing chemotherapeutic drug resistance exhibited in-situ by a solid mass neoplasm of epithelial cell origin. The tumor cells constituting the solid neoplasm have clin. demonstrated resistance in-situ to a single- or multiple-drug treatment regimen, and the resistant tumor cells express both the PDZK1 protein and the cMOAT protein intracellularly. The invention provides antagonistic antibody preps. which inhibit the interaction of PDZK1 and cMOAT proteins intracellularly; and thereby cause a reduction in clin. resistance to the previously administered chemotherapeutic treatment agents.

IC ICM A61K

CC 15-3 (Immunochimistry)

Section cross-reference(s): 1, 3

IT Neoplasm

(epithelial; antagonistic antibodies against PDZK1 protein or cMOAT protein for reducing chemotherapeutic drug resistance in-situ within neoplasms of epithelial cell origin)

IT Neoplasm

(solid, epithelial; antagonistic antibodies against PDZK1 protein or cMOAT protein for reducing chemotherapeutic drug resistance in-situ within neoplasms of epithelial cell origin)

IT 283366-21-2

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antagonistic antibodies against PDZK1 protein or cMOAT protein for reducing chemotherapeutic drug resistance in-situ within neoplasms of epithelial cell origin)

IT 283366-21-2

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

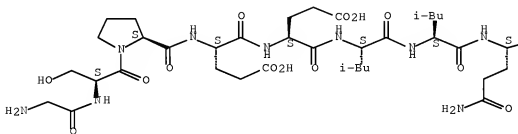
(antagonistic antibodies against PDZK1 protein or cMOAT protein for reducing chemotherapeutic drug resistance in-situ within neoplasms of epithelial cell origin)

RN 283366-21-2 CAPLUS

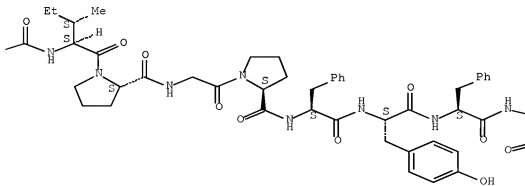
CN L-Phenylalanine, glycyl-L-seryl-L-prolyl-L- α -glutamyl-L- α -glutamyl-L-leucyl-L-leucyl-L-glutamyl-L-isoleucyl-L-prolylglycyl-L-prolyl-L-phenylalanyl-L-tyrosyl-L-phenylalanyl-L-methionyl-L-alanyl-L-lysyl-L- α -glutamyl-L-alanylglycyl-L-isoleucyl-L- α -glutamyl-L-asparaginyl-L-valyl-L-asparaginyl-L-seryl-L-threonyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

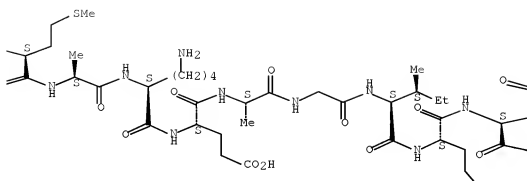
PAGE 1-A



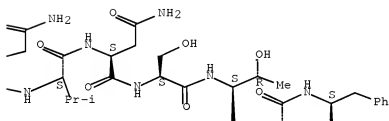
PAGE 1-B



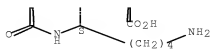
PAGE 1-C



PAGE 1-D

PAGE 2-C
CO₂H

PAGE 2-D



L80 ANSWER 30 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:445977 CAPLUS Full-text

DOCUMENT NUMBER: 133:187662

TITLE: The influence of cytotoxicity of macromolecules and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors

AUTHOR(S): Minko, Tamara; Kopeckova, Pavla; Pozharov, Vitaliy; Jensen, Keith D.; Kopecek, Jindrich

CORPORATE SOURCE: Department of Pharmaceuticals and Pharmaceutical Chemistry, University of Utah, Salt Lake City, UT, USA

SOURCE: Pharmaceutical Research (2000), 17(5), 505-514

CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To study the influence of cytotoxicity of macromols., VEGF gene expression, and vascular permeability on the enhanced permeability and retention (EPR) effect. Mice bearing xenografts of A2780 multidrug resistant human ovarian carcinoma were treated by free doxorubicin (DOX) and N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer-bound DOX (P(GFLG)-DOX), Texas Red (P-TR), and FITC (P-FITC). Antitumor activity, drug distribution in tumor, vascular permeability, VEGF gene expression, and DNA fragmentation were studied. The accumulation of free DOX led to the VEGF gene overexpression and increased the vascular permeability, which in turn enhanced the drug accumulation in the same location. This pos. feedback loop led to a highly inhomogeneous distribution of the drug within the tumor. In contrast, P(GFLG)-DOX down-regulated the VEGF gene and decreased vascular permeability. This neg. feedback seemed to prevent addnl. drug accumulation in dead necrotic tissue, resulting in a more uniform drug distribution and enhanced the antitumor activity P(GFLG)-DOX. The EPR effect significantly differed for macromols. containing DOX when compared to macromols. without drug. The cytotoxicity of P(GFLG)-DOX amplified the EPR effect, led to a more homogeneous distribution of the drug, increased the average drug concentration in tumor and augmented its efficacy.

CC 1-6 (Pharmacology)

IT Ovary, neoplasm

Ovary, neoplasm

(carcinoma, inhibitors; influence of cytotoxicity of macromols. and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors)

IT Antitumor agents

(ovary carcinoma; influence of cytotoxicity of macromols. and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors)

IT Antitumor agents

(resistance to; influence of cytotoxicity of macromols. and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors)

IT 23214-92-8D, Doxorubicin, conjugate with HPMA copolymer 57950-81-9D,

conjugated with FITC 82354-19-6D, Texas Red, conjugate with HPMA

copolymer 86742-37-2D, conjugate with HPMA copolymer

106424-12-4D, conjugated with doxorubicin 289690-97-7D,

conjugates with Texas Red

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES

(Uses)

(influence of cytotoxicity of macromols. and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors)

IT 100424-72-4L, conjugated with doxorubicin

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(influence of cytotoxicity of macromols. and of VEGF gene modulated vascular permeability on the enhanced permeability and retention effect in resistant solid tumors)

RN 100424-72-4 CAPLUS

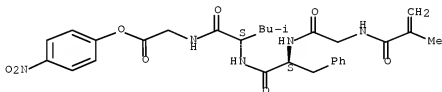
CN Glycine, N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-L-phenylalanyl-L-leucyl-, 4-nitrophenyl ester, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (CA INDEX NAME)

CM 1

CRN 100424-71-3

CMF C29 H35 N5 O8

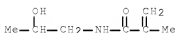
Absolute stereochemistry.



CM 2

CRN 21442-01-3

CMF C7 H13 N O2



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 31 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:4384 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 132:30486

TITLE: Combined treatment with goserelin and tamoxifen in patients with advanced chemotherapy resistant ovarian cancer

AUTHOR(S): Hofstra, L. S.; Mourits, M. J. E.; De Vries, E. G. E.; Mulder, N. H.; Willemse, P. H. B.

CORPORATE SOURCE: Departments of Medical Oncology, University Hospital Groningen, 30.0019700 RB, Neth.

SOURCE: Anticancer Research (1999), 19(4C),

3627-3630

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this study was to determine the response in patients with recurrent, chemotherapy-resistant ovarian cancer to a combination of the LHRH-analog goserelin and tamoxifen. Patients and methods: Twenty-five patients with recurrent, chemotherapy resistant ovarian cancer received a combination of goserelin and tamoxifen until clin. or serol. evidence of progression as measured by serum CA-125 levels. Suppression of LH, FSH and prolactin levels in this group were compared with a second group of ten patients treated with decapeptyl for the same indication. Results: The combination was well tolerated. The median progression free survival amounted to five (range 2-96+) months and overall survival to eight (range 3-96+) months. One of the responding patients is still alive without progression at 8 yr. With this combination the median levels of LH and FSH were markedly suppressed, to resp. 2.6% and 3.7% of baseline values. With decapeptyl the LH levels were also suppressed, but the resulting FSH levels were significantly higher. PA combination of goserelin and tamoxifen in patients with relapsed ovarian cancer can not be recommended as standard therapy, but may result in long-term survival in individual patients.

CC 1-6 (Pharmacology)
Section cross-reference(s): 2

IT Ovary, neoplasm
Ovary, neoplasm
(inhibitors; combined treatment with goserelin and tamoxifen in humans with advanced chemotherapy resistant ovarian cancer)

IT Antitumor agents
Antitumor agents
(ovary; combined treatment with goserelin and tamoxifen in humans with advanced chemotherapy resistant ovarian cancer)

IT 10540-29-1, Tamoxifen 65807-02-5, Goserelin
RL: ADV (Adverse effect, including toxicity); EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combined treatment with goserelin and tamoxifen in humans with advanced chemotherapy resistant ovarian cancer)

IT 57773-63-4, Decapeptyl
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combined treatment with goserelin and tamoxifen in humans with advanced chemotherapy resistant ovarian cancer)

IT 65807-02-5, Goserelin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

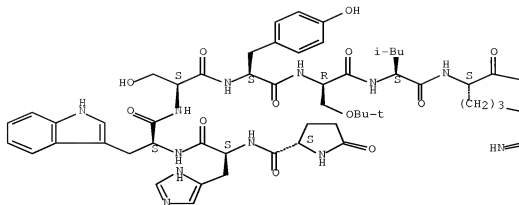
(combined treatment with goserelin and tamoxifen in humans with advanced chemotherapy resistant ovarian cancer)

RN 65807-02-5 CAPLUS

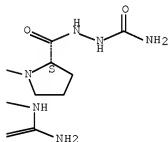
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 57773-63-4, Decapeptyl

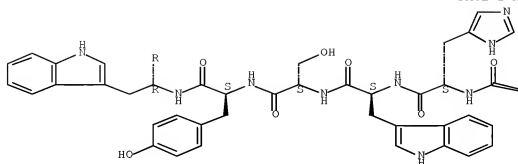
RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (combined treatment with goserelin and tamoxifen in humans with
 advanced chemotherapy resistant ovarian cancer)

RN 57773-63-4 CAPLUS

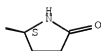
CN Luteinizing hormone-releasing factor (swine), 6-D-tryptophan- (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (-).

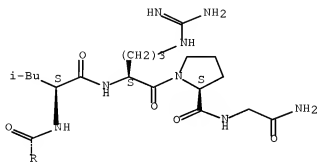
PAGE 1-A



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 32 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:819523 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 132:59135

TITLE: Fitness assay and associated methods, and applications

to drug resistance and HIV protease inhibitors and other drugs with reduced resistance

Erickson, John W.; Gulnik, Sergei V.

INVENTOR(S): United States of America, Represented by the Secretary, Department of Health and Human Services, USA

SOURCE: PCT Int. Appl., 119 pp.

DOCUMENT TYPE: CODEN: PIXXD2
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: English 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967417	A2	19991229	WO 1999-US14119	19990623 <--
WO 9967417	A3	20000928		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2336160	A1	19991229	CA 1999-2336160	19990623 <--
AU 9948280	A	20000110	AU 1999-48280	19990623 <--
AU 771780	B2	20040401		
EP 1088098	A2	20010404	EP 1999-931861	19990623 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2002518063	T	20020625	JP 2000-556057	19990623 <--
AU 2004200629	A1	20040311	AU 2004-200629	20040218 <--
AU 2004200629	B2	20070419		
US 20050158713	A1	20050721	US 2005-30632	20050106 <--
AU 2007203321	A1	20070809	AU 2007-203321	20070717
US 20080085918	A1	20080410	US 2007-870931	20071011 <--
PRIORITY APPLN. INFO.:			US 1998-90393P	P 19980623 <--
			AU 1999-48280	A3 19990623 <--
			WO 1999-US14119	W 19990623 <--
			US 2001-720276	A1 20010307 <--
			AU 2004-200629	A3 20040218

OTHER SOURCE(S): MARPAT 132:59135

GI For diagram(s), see printed CA Issue.

AB The invention provides an assay for determining the biochem. fitness of a biochem. species in a mutant replicating biol. entity relative to its predecessor. The invention further provides a continuous fluorogenic assay for measuring the anti-HIV protease activity of protease inhibitor. The invention also provides a method of administering a therapeutic compound that reduces the chances of the emergence of drug resistance in therapy. The invention also provides a compound AXQN(R2)CH[(CH2)mR3]CH(R4)CH2N(R5)(WR 6) [A = Q1, Q2, Q3, Q4; R1, R2, R3, R5, R6 = H, (substituted and/or heteroatom-bearing) alkyl, alkenyl, alkynyl, or cyclic group; Y, Z = CH2, O, S, SO, SO2, amino, amides, carbamates, ureas, or thiocarbonyl derivs. thereof, optionally substituted with an alkyl, alkenyl, or alkynyl group; n = 1-5; X = bond, (substituted) methylene or ethylene, amino, O, S; Q = C(O), C(S), SO2; m = 0-6; R4 = OH, =O (keto), NH2, alkylamino, including esters, amides, and salts thereof; W = C(O), C(S), S(O), SO2; Optionally, R5 and R6, together with the NW bond comprise a macrocyclic ring], or a pharmaceutically acceptable salt, a prodrug, a composition, or an ester thereof.

IC ICM C12Q001-00

CC 1-1 (Pharmacology)

Section cross-reference(s): 28, 63

IT Anti-infective agents

Antibacterial agents

Antimalarials

Antitumor agents

Antiviral agents
Bacteria (Eubacteria)
Drug resistance
Drugs
Enzyme kinetics
Fluorometry
Human immunodeficiency virus
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Michaelis constant
Multidrug resistance
Mutation
Neoplasm
Plasmodium (malarial genus)
Resolution (separation)
Retroviridae
Virus

(fitness assay and associated methods, and applications to drug resistance and HIV protease inhibitors and other drugs with reduced resistance)

IT 128340-45-4 253274-32-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (fitness assay and associated methods, and applications to drug resistance and HIV protease inhibitors and other drugs with reduced resistance).

IT 128340-45-4 253274-32-7

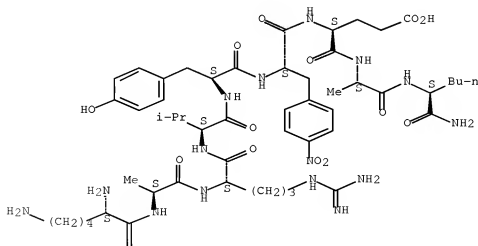
RL: EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (fitness assay and associated methods, and applications to drug resistance and HIV protease inhibitors and other drugs with reduced resistance).

RN 128340-45-4 CAPLUS

L-Norleucinamide, L-lysyl-L-alanyl-L-arginyl-L-valyl-L-tyrosyl-4-nitro-L-phenylalanyl-L- α -glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

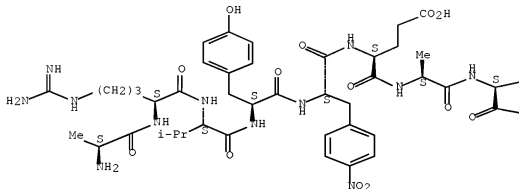


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RN 253274-32-7 CAPLUS
 CN L-Norleucinamide, L-alanyl-L-arginyl-L-valyl-L-tyrosyl-4-nitro-L-phenylalanyl-L- α -glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

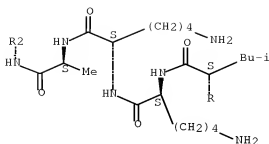
—Bu-n

—NH₂

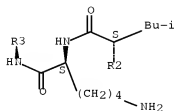
L80 ANSWER 33 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1999:671008 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 131:272185
 TITLE: Preparation of digestion resistant glyoxylated arginine-containing lytic peptides
 Julian, Gordon R.; Jaynes, Jesse M.
 INVENTOR(S): Demegen, Inc., USA
 PATENT ASSIGNEE(S): U.S., 11 pp., Cont.-in-part of U. S. 5,561,107.
 SOURCE: CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 11
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968904	A	19991019	US 1995-475328	19950607 <--
US 5561107	A	19961001	US 1994-231730	19940420 <--
PRIORITY APPLN. INFO.:			US 1993-39620	B2 19930604 <--
			US 1993-148491	B2 19931108 <--
			US 1993-148889	B2 19931108 <--
			US 1994-225476	B2 19940408 <--
			US 1994-231730	A2 19940420 <--
AB	Non-neurotoxin, arginine residue-containing lytic peptides were glyoxylated at the guanidino group of arginine to enhance resistance to tryptic, chymotryptic, and aminopeptidase digestion. Thus, Phe-Ala-Arg-Arg-Leu-Ala-Arg-Arg-Leu-Ala-Arg-Arg-Leu-Ala-Arg-Arg-Leu-Ala-Leu (Shiva 10R) in 80% pyridine was treated with aqueous NaHCO3/NaOH and then 30% glyoxal suspension in aqueous NaHCO3 to give the glyoxylated peptide. The latter was fully protected from hydrolysis by trypsin, whereas the unmodified peptide was susceptible to hydrolysis. In general, the modified peptides showed bacteriolytic activity at 10 µM.			
IC	ICM A61K038-10			
	ICS A61K038-16; C07K007-08; C07K014-00			
INCL	514012000			
CC	34-3 (Amino Acids, Peptides, and Proteins)			
	Section cross-reference(s): 10			
IT	Antibacterial agents			
	Antitumor agents			
	Antiviral agents			
	Digestion, chemical			
	Fungicides			
	Infection			
	(preparation of digestion resistant glyoxylated arginine-containing lytic peptides)			
IT	133084-63-6 162136-51-3 162136-52-9			
	162136-53-0 162136-54-1 162136-55-2			
	162136-56-3 162136-57-4 162136-58-5			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)			
	(preparation of digestion resistant glyoxylated arginine-containing lytic peptides)			
IT	107-22-2, Glyoxal 170846-30-7			
	RL: RCT (Reactant); RACT (Reactant or reagent)			
	(preparation of digestion resistant glyoxylated arginine-containing lytic peptides)			
IT	170846-30-7DE, glyoxylated			
	RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)			
	(preparation of digestion resistant glyoxylated arginine-containing lytic peptides)			
IT	133084-63-6 162136-51-3 162136-52-9			
	162136-53-0 162136-54-1 162136-56-3			
	162136-58-5			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)			
	(preparation of digestion resistant glyoxylated arginine-containing lytic peptides)			
RN	133084-63-6 CAPLUS			
CN	L-Leucine, L-phenylalanyl-L-alanyl-L-leucyl-L-alanyl-L-leucyl-L-lysyl-L-alanyl-L-leucyl-L-lysyl-L-lysyl-L-alanyl-L-leucyl-L-lysyl-L-leucyl-L-lysyl-L-lysyl-L-alanyl-L-leucyl-L-lysyl-L-lysyl-L-alanyl- (CA INDEX NAME)			

PAGE 4-A



PAGE 5-A

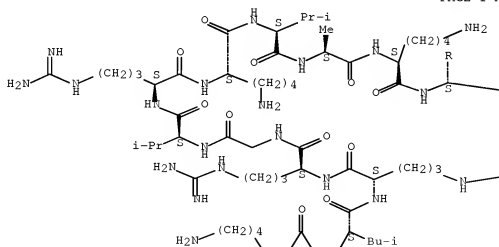


RN 162136-51-8 CAPLUS

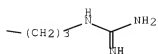
CN L-Arginine, L-phenylalanyl-L-alanyl-L-valylglycyl-L-leucyl-L-arginyl-L-alanyl-L-isoleucyl-L-lysyl-L-arginyl-L-alanyl-L-leucyl-L-lysyl-L-lysyl-L-leucyl-L-arginyl-L-arginylglycyl-L-valyl-L-arginyl-L-lysyl-L-valyl-L-alanyl-L-lysyl-L-arginyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

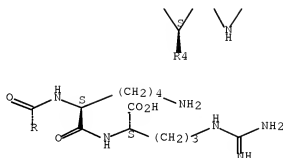
PAGE 1-A



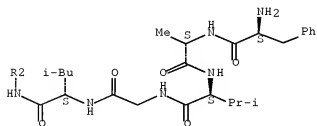
PAGE 1-B



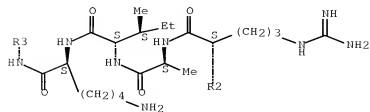
PAGE 2-A



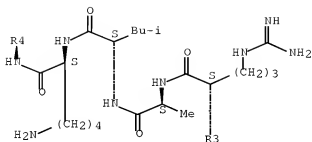
PAGE 3-A



PAGE 4-A



PAGE 5-A



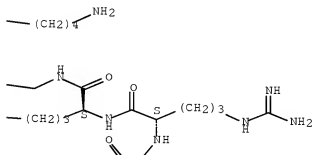
RN 162136-52-9 CAPLUS

CN L-Alanine, L-phenylalanyl-L-alanyl-L-valylglycyl-L-leucyl-L-arginyl-L-alanyl-L-isoleucyl-L-lysyl-L-arginyl-L-alanyl-L-leucyl-L-lysyl-L-lysyl-L-leucyl-L-arginyl-L-arginylglycyl-L-valyl-L-arginyl-L-lysyl-L-valyl- (9CI)
(CA INDEX NAME)

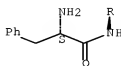
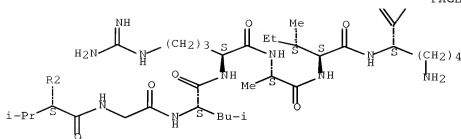
Absolute stereochemistry.

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

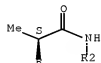
PAGE 1-B



PAGE 3-A

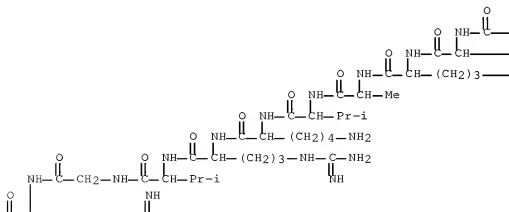


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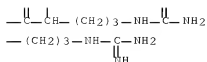


RN 162136-53-0 CAPLUS
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PAGE 1-C



PAGE 2-C

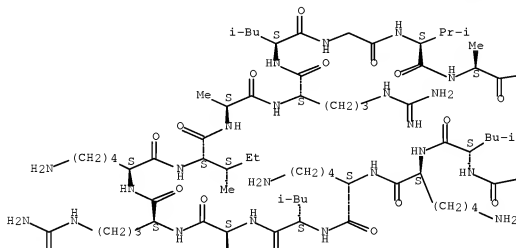


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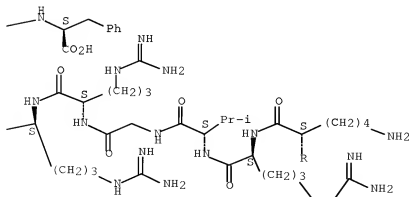
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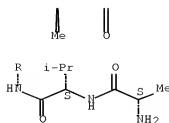
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





PAGE 2-A

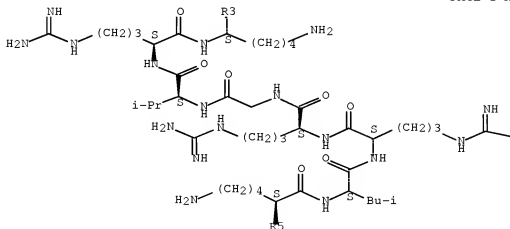


PAGE 2-B

RN 162136-56-3 CAPLUS

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Absolute stereochemistry.

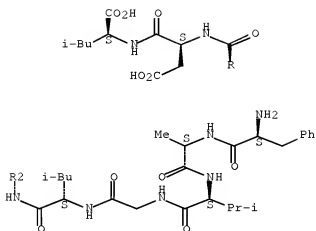


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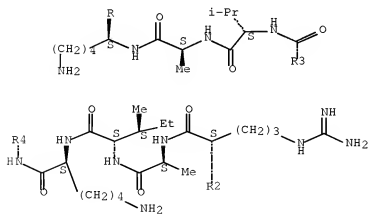
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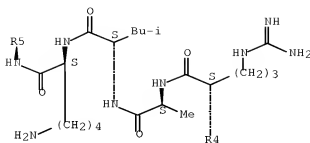
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PAGE 3-A

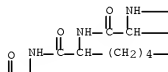


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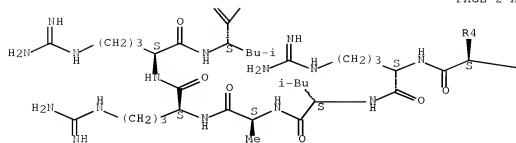


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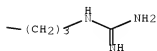
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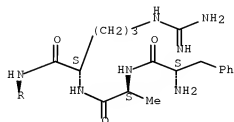
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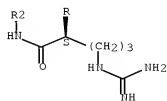
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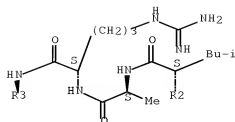
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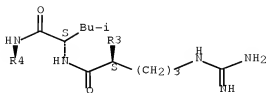
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PAGE 5-A



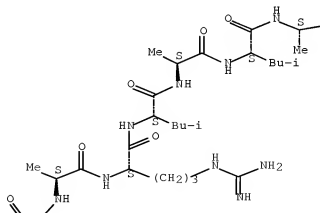
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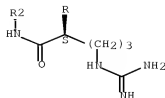
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of digestion resistant glyoxylated arginine-containing lytic
 peptides)
 RN 170846-30-7 CAPLUS
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 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

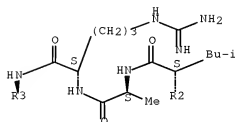
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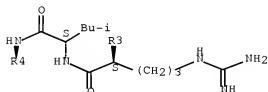
PAGE 4-A



PAGE 5-A



PAGE 6-A



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 34 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:425747 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 131:54018

TITLE: Combination of benzocycloheptapyridine compound
farnesyl protein transferase inhibitors and
antineoplastic drugs for treating proliferative
diseases

INVENTOR(S): Bishop, Walter R.; Catino, Joseph J.; Doll, Ronald J.;
Ganguly, Ashit; Girijavallabhan, Viyyoor; Kirschmeier,
Paul; Liu, Ming; Nielsen, Loretta L.; Cutler, David L.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932114	A1	19990701	WO 1998-US26224	19981221 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9811734	A	19990621	ZA 1998-11734	19981221 <--
CA 2315693	A1	19990701	CA 1998-2315693	19981221 <--
AU 9919072	A	19990712	AU 1999-19072	19981221 <--
AU 756762	B2	20030123		
BR 9814419	A	20001010	BR 1998-14419	19981221 <--
EP 1041985	A1	20001011	EP 1998-963829	19981221 <--
EP 1041985	B1	20060215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
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HU 2001002473	A2	20020128	HU 2001-2473	19981221 <--
HU 2001002473	A3	20030728		
CN 1129431	C	20031203	CN 1998-813742	19981221 <--
TW 581763	B	20040401	TW 1998-87121355	19981221 <--
NZ 504928	A	20041224	NZ 1998-504928	19981221 <--
AT 317697	T	20060315	AT 1998-963829	19981221 <--
ES 2255196	T3	20060616	ES 1998-963829	19981221 <--
PT 1041985	T	20060731	PT 1998-963829	19981221 <--
SK 285584	B6	20070405	SK 2000-898	19981221 <--
CZ 298511	B6	20071024	CZ 2000-2236	19981221 <--
NO 2000003229	A	20000822	NO 2000-3229	20000621 <--
MX 2000PA06257	A	20010118	MX 2000-PA6257	20000622 <--
PRIORITY APPLN. INFO.:			US 1997-996027	A 19971222 <--
			US 1998-143529	A 19980828 <--
			US 1998-181969	A 19981029 <--
			WO 1998-US26224	W 19981221 <--

OTHER SOURCE(S): MARPAT 131:54018

- AB Methods are provided for treating proliferative diseases, especially cancers, comprising administering a farnesyl protein transferase inhibitor in conjunction with an antineoplastic agent and/or radiation therapy.
- IC ICM A61K031-44
ICS A61K031-495
- CC 1-6 (Pharmacology)
Section cross-reference(s): 63
- IT Microtubule
(agents affecting; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(bladder carcinoma; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(carcinoma; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative

- disease)
- IT Antitumor agents
(colon; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Intestine, neoplasm
Intestine, neoplasm
(colorectal, inhibitors; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(colorectal; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
Cytotoxic agents
Drug resistance
Gamma ray
Myelodysplastic syndromes
Peptidomimetics
Radiotherapy
(farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Thyroid gland, neoplasm
(follicular cell carcinoma, metastasis, inhibitors; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(glioma; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Lung, neoplasm
Lung, neoplasm
Ovary, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
(inhibitors; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Lung, neoplasm
Lung, neoplasm
(large-cell carcinoma, inhibitors; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(lung large-cell carcinoma; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
Antitumor agents
(lung; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(mammary gland; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(melanoma; farnesyl protein transferase inhibitor combination with

- antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(myelogenous leukemia; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
Antitumor agents
(ovary; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
Antitumor agents
(pancreas; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(prostate gland; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT Antitumor agents
(thyroid gland follicular cell carcinoma, metastasis; farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)
- IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-24-8, Prednisolone 50-44-2, 6-Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-18-3, Triethylenemelamine 51-21-8, 5-Fluorouracil 51-75-2, Chlormethine 52-24-4 53-03-2, Prednisone 53-19-0, Mitotane 54-91-1, Pipobroman 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 57-63-6, 17 α -Ethinylestradiol 58-18-4, Methyltestosterone 58-22-0, Testosterone 59-05-2, Methotrexate 66-75-1, Uracil mustard 68-96-2, Hydroxyprogesterone 71-58-9, Medroxyprogesteroneacetate 76-43-7, Fluoxymesterone 83-43-2, Methylprednisolone 124-94-7, Triamcinolone 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, 6-Thioguanine 154-93-8, Carmustine 305-03-3, Chlorambucil 521-12-0, Dromostanolone propionate 569-57-3, Chlorotrianisene 595-33-5, Megestrol acetate 645-05-6, Hexamethylmelamine 671-16-9, Procarbazine 865-21-4, Vinblastine 968-93-4, Testolactone 2998-57-4, Estramustine 3778-73-2, Ifosfamide 3964-78-1D, derivs. 4342-03-4, Dacarbazine 9015-68-3, L-Asparaginase 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 14769-73-4, Levamisole 15663-27-1, Cisplatin 18378-89-7, Mithramycin 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33069-62-4D, Paclitaxel, derivs. 33419-42-0, Etoposide 41575-94-4, Carboplatin 51264-14-3, Amsacrine 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 65271-80-9, Mitoxantrone 65897-02-5, Goserelin 75607-67-9, Fludarabine phosphate 82413-20-5, Droloxifene 84449-90-1, Raloxifene 85622-93-1, Temozolomide 89778-26-7, Toremifene 95058-81-4, Gemcitabine 100286-90-6, CPT-11 112809-51-5, Letrozole 114977-28-5, Taxotere 120511-73-1, Anastrozole 125317-39-7, Navelbine 154361-50-9, Capecitabine 193275-84-2
- RL: EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)

IT 53714-56-0, Leuprolide 65807-02-5, Goserelin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

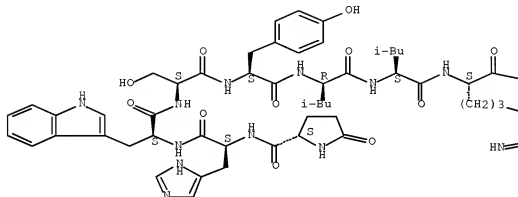
(farnesyl protein transferase inhibitor combination with antineoplastic drug or radiotherapy for treatment of proliferative disease)

RN 53714-56-0 CAPLUS

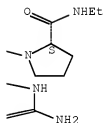
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-D-leucine-9-(N-ethyl-L-prolinamide)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

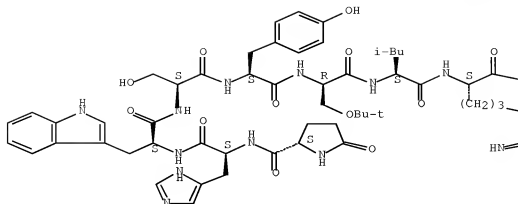


RN 65807-02-5 CAPLUS

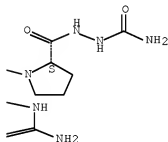
CN 1-9-Luteinizing hormone-releasing factor (swine), 6-[O-(1,1-dimethylethyl)-D-serine]-, 2-(aminocarbonyl)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 35 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1999:3295 CAPLUS Full-text
 DOCUMENT NUMBER: 130:51355
 TITLE: Antigen-binding sites of antibody molecules specific for cancer antigens
 INVENTOR(S): Ring, David B.
 PATENT ASSIGNEE(S): Chiron Corporation, USA
 SOURCE: U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 323,566, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5849877	A	19981215	US 1995-483199	19950607 <--
US 5959084	A	19990928	US 1995-480527	19950607 <--
US 6106833	A	20000822	US 1997-968335	19971112 <--
US 6143873	A	20001107	US 1999-337800	19990622 <--

PRIORITY APPLN. INFO.:

US 1990-605399	B1 19901029 <--
US 1993-141375	B1 19931022 <--
US 1994-323566	B2 19941017 <--
US 1995-452809	B1 19950530 <--
US 1995-480527	A1 19950607 <--

AB Novel compns. are provided that are derived from antigen-binding sites of Igs having affinity for cancer antigens. The compns. exhibit immunol. binding properties of antibody mols. capable of binding specifically to a human tumor cell displaying a MDR phenotype. A number of synthetic mols. are provided that include CDR and FR regions derived from same or different Ig moieties. Also provided are single chain polypeptides wherein VH and VL domains are attached by a single polypeptide linker. The sFv mols. can include ancillary polypeptide moieties which can be bioactive, or which provide a site of attachment for other useful moieties. The compns. are useful in specific binding assays, affinity purification schemes, drug or toxin targeting, imaging, and genetic or immunol. therapeutics for various cancers. The invention thus provides novel polypeptides, the DNAs encoding those polypeptides, expression cassettes comprising those DNAs, and methods of inducing the production of the polypeptides. Mouse monoclonal anti-human MDR1 gene protein antibody 15D3 was raised, and peptides derived from heavy and light chain variable region of the antibody were used for the disclosed purposes.

IC ICM C07K016-00
ICS C12N005-00; C12N015-00; C12P021-04

INCL 530387100

CC 15-3 (Immunochemistry)

IT Antitumor agents

Drug targeting

Gene therapy

Immunotherapy

Protein sequences

(antibody peptides specific to human tumor cell displaying multiple drug resistance are used for drug or toxin targeting, tumor imaging, genetherapy or immunotherapy)

IT Neoplasm

(diagnosis; antibody peptides specific to human tumor cell displaying multiple drug resistance are used for drug or toxin targeting, tumor imaging, genetherapy or immunotherapy)

IT 158329-15-8 217495-46-0 217495-47-1

217495-48-2 217495-49-3 217495-50-6

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibody peptides specific to human tumor cell displaying multiple drug resistance are used for drug or toxin targeting, tumor imaging, genetherapy or immunotherapy)

IT 158329-15-8 217495-46-0 217495-47-1

217495-48-2 217495-49-3 217495-50-6

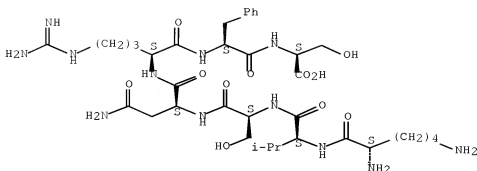
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibody peptides specific to human tumor cell displaying multiple drug resistance are used for drug or toxin targeting, tumor imaging, genetherapy or immunotherapy)

RN 158329-15-8 CAPLUS

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(CA INDEX NAME)

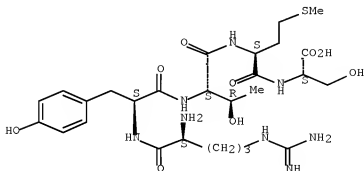
Absolute stereochemistry.



RN 217495-46-0 CAPLUS

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Absolute stereochemistry.

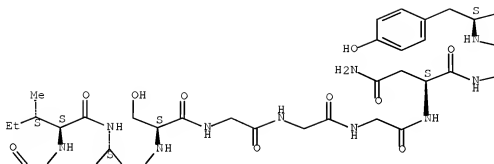


RN 217495-47-1 CAPLUS

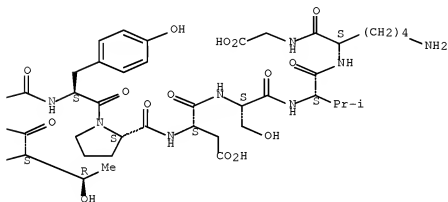
CN Glycine, L-threonyl-L-isoleucyl-L-seryl-L-serylglycylglycylglycyl-L-asparaginyl-L-threonyl-L-tyrosyl-L-tyrosyl-L-prolyl-L-α-aspartyl-L-seryl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

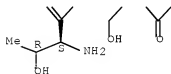
PAGE 1-A



PAGE 1-B



PAGE 2-A

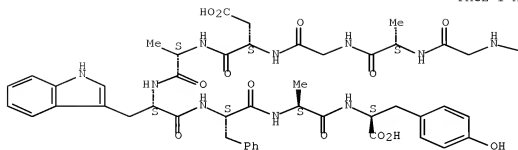


RN 217495-48-2 CAPLUS

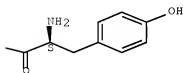
CN L-Tyrosine, L-tyrosylglycyl-L-alanylglycyl-L- α -aspartyl-L-alanyl-L-tryptophyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

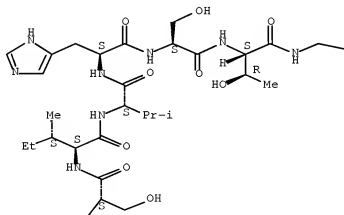


RN 217495-49-3 CAPLUS

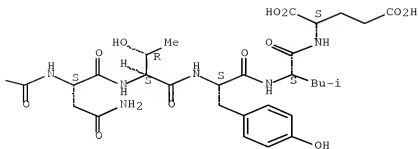
CN L-Glutamic acid, L-arginyl-L-seryl-L-seryl-L-glutaminyl-L-seryl-L-isoleucyl-L-valyl-L-histidyl-L-seryl-L-threonylglycyl-L-asparaginyl-L-threonyl-L-tyrosyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

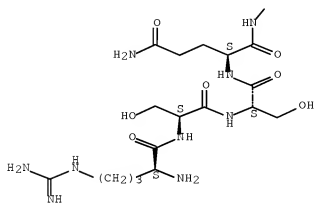
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PAGE 1-B



PAGE 2-A

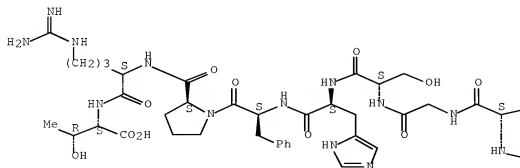


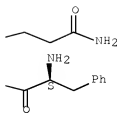
RN 217495-50-6 CAPLUS

CN L-Threonine, L-phenylalanyl-L-glutaminyglycyl-L-seryl-L-histidyl-L-phenylalanyl-L-prolyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 36 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:542006 CAPLUS Full-text

DOCUMENT NUMBER: 129:298630

ORIGINAL REFERENCE NO.: 129:60793a,60796a

TITLE: Reversal of clinical resistance to LHRH analog in metastatic prostate cancer by the pineal hormone melatonin: efficacy of LHRH analog plus melatonin in patients progressing on LHRH analog alone

AUTHOR(S): Lissoni, Paolo; Cazzaniga, Marina; Tancini, Gabriele; Scardino, Epifanio; Musci, Roberto; Barni, Sandro; Maffezzini, Massimo; Meroni, Tiziano; Rocco, Francesco; Conti, Ario; Maestroni, George
CORPORATE SOURCE: Division of Radiation Oncology, San Gerardo Hospital, Milan, I-20052, Italy

SOURCE: European Urology (1997), 31(2), 178-181

CODEN: EUURAV; ISSN: 0302-2838

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Exptl. and preliminary clin. studies have suggested that the pineal hormone melatonin (MLT) may stimulate hormone receptor expression on both normal and cancer cells. Moreover, MLT has appeared to inhibit the growth of some cancer cell lines, including prostate cancer, either by exerting a direct cytostatic action, or by decreasing the endogenous production of some tumor growth factors, such as prolactin (PRL) and insulin-like growth factor-1 (IGF-1). On this basis, a study was carried out to evaluate the clin. efficacy of a neuroendocrine combination consisting of the LHRH analog triptorelin plus MLT in metastatic prostate cancer progressing on triptorelin alone. The study including 14 consecutive metastatic prostate cancer patients with poor clin. conditions (median age: 70.5 yr; median PS: 50%), refractory or resistant to a previous therapy with the LHRH analog triptorelin alone. Triptorelin was injected i.m. at 3.75 mg every 28 days, and MLT was given orally at 20 mg/day in the evening every day until progression, starting 7 days prior to triptorelin. A decrease in PSA serum levels greater than 50% was obtained in 8/14 (57%) patients. Moreover, PSA mean concns. significantly decreased on therapy of triptorelin plus MLT. In addition, a normalization of platelet number was obtained in 3/5 patients with persistent thrombocytopenia prior to study. Mean serum levels of both PRL and IGF-1 significantly decreased on therapy. Finally, a survival longer than 1 yr was achieved in 9/14 (64%) patients. This preliminary study would suggest that the concomitant

administration of the pineal hormone MLT may overcome the clin. resistance to LHRH analogs and improve the clin. conditions in metastatic prostatic cancer patients.

CC 2-10 (Mammalian Hormones)

Section cross-reference(s): 1

IT Antitumor agents

(prostate gland; melatonin plus LHRH analog treatment of men with LHRH analog-resistant metastatic prostate cancer)

IT Antitumor agents

(resistance to; melatonin plus LHRH analog treatment of men with LHRH analog-resistant metastatic prostate cancer)

IT 73-31-4, Melatonin 57773-63-4, Triptorelin

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(melatonin plus LHRH analog treatment of men with LHRH analog-resistant metastatic prostate cancer)

IT 57773-63-4, Triptorelin

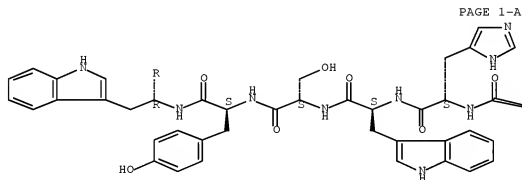
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(melatonin plus LHRH analog treatment of men with LHRH analog-resistant metastatic prostate cancer)

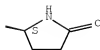
RN 57773-63-4 CAPLUS

CN Luteinizing hormone-releasing factor (swine), 6-D-tryptophan- (CA INDEX NAME)

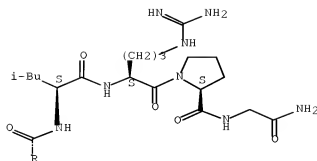
Absolute stereochemistry. Rotation (-).



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 37 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:541438 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 129:254546

ORIGINAL REFERENCE NO.: 129:51670h,51671a

TITLE: Linear and cyclic peptides as substrates and modulators of P-glycoprotein: peptide binding and effects on drug transport and accumulation
 AUTHOR(S): Sharom, Frances J.; Lu, Peihua; Liu, Ronghua; Yu, Xiaohong

CORPORATE SOURCE: Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry, Department of Chemistry and Biochemistry, University of Guelph, Guelph, ON, N1G 2W1, Can.

SOURCE: Biochemical Journal (1998), 333(3), 621-630
 CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB One cause of multidrug resistance (MDR) in human cancers is the overexpression of the P-glycoprotein multidrug transporter, a member of the ABC superfamily of membrane proteins. Natural products and chemotherapeutic drugs are pumped out of the cell by P-glycoprotein in an ATP-dependent fashion. There is growing evidence that many hydrophobic peptides are also P-glycoprotein substrates. With the use of a fluorescence-quenching assay, the authors have shown that some linear and cyclic hydrophobic peptides interact with P-glycoprotein, whereas others do not. The measured values of the quenching constant, Kq, for interaction of peptides with P-glycoprotein ranged from 200 nM for cyclosporine A to 138 μM for the tripeptide N-acetyl-leucyl-leucyl-norleucinal. Peptides that interacted with P-glycoprotein in the fluorescence assay also blocked colchicine transport into plasma membrane vesicles from MDR cells. The values of Dm, the peptide concentration causing 50% inhibition of drug uptake, were highly correlated with the values of Kq, over three orders of magnitude. The P-glycoprotein ATPase stimulation/inhibition profile of the peptides was not helpful in making a quant. assessment of the ability of a peptide to interact with P-glycoprotein or to block drug transport. Some hydrophobic peptides were able to restore accumulation in MDR cells of the chemotherapeutic drug daunorubicin and the fluorescent dye rhodamine 123 to the levels observed in the drug-sensitive parent. Peptides that interacted with P-glycoprotein also displayed a relatively low overall toxicity to intact MDR cells, and inhibited drug transport at concns. below the toxic range.

Hydrophobic peptides should be given serious consideration for development as clin. chemosensitizing agents.

CC 1-6 (Pharmacology)

IT Antitumor agents

Multidrug resistance

(linear and cyclic peptides as substrates and modulators of

P-glycoprotein in relation to binding and effects on drug transport and accumulation and use as chemosensitizing agents for multidrug resistant cancer)

IT 2001-95-8, Valinomycin 9076-44-2, Chymostatin 11029-61-1, Gramicidin A 17090-79-8, Monensin 20449-79-0, Melittin 26048-05-5, Beauvericin 26305-03-3, Pepstatin A 27061-78-5, Alamethicin 28380-24-7, Nigericin 51724-57-3, Pepsinostreptin 55123-66-5, Leupeptin 59865-13-3, Cyclosporine A 81344-47-0 83903-28-0 110044-82-1 110115-07-6 186042-32-0

RL: EAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(linear and cyclic peptides as substrates and modulators of

P-glycoprotein in relation to binding and effects on drug transport and accumulation and use as chemosensitizing agents for multidrug resistant cancer)

IT 20449-79-0, Melittin 26305-03-3, Pepstatin A 51724-57-3, Pepsinostreptin 83903-28-0 186042-32-0

RL: EAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

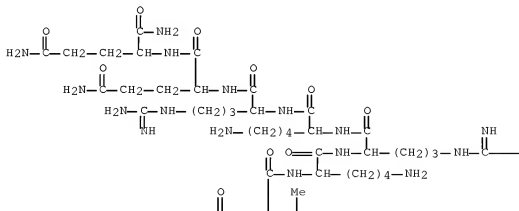
(linear and cyclic peptides as substrates and modulators of

P-glycoprotein in relation to binding and effects on drug transport and accumulation and use as chemosensitizing agents for multidrug resistant cancer)

RN 20449-79-0 CAPLUS

CN Melittin (honeybee) (CA INDEX NAME)

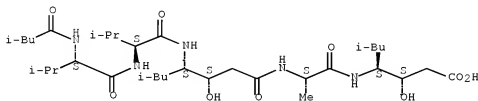
PAGE 1-A



RN 26305-03-3 CAPLUS

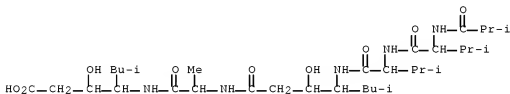
CN L-Alaninamide, N-(3-methyl-1-oxobutyl)-L-valyl-L-valyl-(3S,4S)-4-amino-3-hydroxy-6-methylheptanoyl-N-[(1S)-1-[(1S)-2-carboxy-1-hydroxyethyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 51724-57-3 CAPLUS

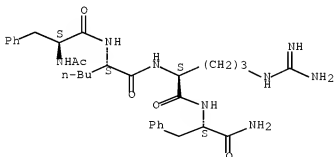
CN L-Alaninamide, N-(2-methyl-1-oxopropyl)-L-valyl-L-valyl-(3S,4S)-4-amino-3-hydroxy-6-methylheptanoyl-N-[(1S)-1-[(1S)-2-carboxy-1-hydroxyethyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)



RN 83903-28-0 CAPLUS

CN L-Phenylalaninamide, N-acetyl-L-phenylalanyl-L-norleucyl-L-arginyl- (CA INDEX NAME)

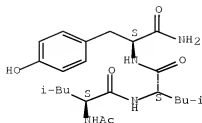
Absolute stereochemistry.



RN 186042-32-0 CAPLUS

CN L-Tyrosinamide, N-acetyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 38 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:517843 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 129:270115

ORIGINAL REFERENCE NO.: 129:54893a,54896a

TITLE: Platelet agonists induce Ca²⁺ transients in tumor cells by opening distinct receptor-operated channels: an effect unrelated to the presence of classical multi-drug resistance phenotype

AUTHOR(S): Moroni, M.; Porta, C.; Tua, A.; Magnone, S.; Grignani, G.

CORPORATE SOURCE: Department of Internal Medicine, University of Pavia, Pavia, Italy

SOURCE: Cancer Journal (1998), 11(3), 141-146

CODEN: CANJEI; ISSN: 0765-7846

PUBLISHER: Association pour le Developpement de la Communication Cancerologique

DOCUMENT TYPE: Journal

LANGUAGE: English

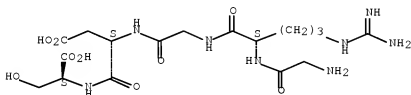
AB Modulation of the cytoplasmic calcium concentration is a mechanism of signal transduction regulating several biol. phenomena and may also play a role in the stimulation of cell proliferation. In the present study we have investigated the effect of different platelet agonists on cytoplasmic Ca²⁺ levels in tumor cells with or without the multi-drug resistance (MDR) phenotype and the effects of verapamil on agonist induced Ca²⁺ transients and on in-vitro tumor cell growth. LoVo cells and doxorubicin-resistant LoVoDx cells, derived from a human colon adenocarcinoma, were cultured in vitro using standard methods. Cytoplasmic Ca²⁺ levels in aequorin-loaded tumor cells were determined in a Platelet Ionized Calcium Aggregometer. ADP, GRGDS, PAF, collagen and thrombin were able to induce Ca²⁺ transients in both cell lines, while U46619, a thromboxane A₂ mimetic agent, PDGF and carbachol were not. Tumor cells of both cell lines became refractory to thrombin after the first addition, but remained sensitive to the other inducers. Furthermore, the calcium channel blocker verapamil significantly inhibited thrombin-induced Ca²⁺ fluxes in both LoVo cells and LoVoDx cells and had no significant effect on Ca²⁺ movements induced by the other agonists. Finally, the drug inhibited the in-vitro growth of both cell lines in a dose-dependent manner, with an effect more evident in resistant cells. These data may help to explain the ability of verapamil to reverse the MDR phenotype and may contribute to identifying new mechanisms for the two-way interaction of tumors with the hemostatic system.

CC 1-6 (Pharmacology)

IT Antitumor agents

(resistance to; platelet agonists induce Ca²⁺ transients in tumor cells by opening receptor-operated channels, effect unrelated to presence of multi-drug resistance phenotype)

IT	52-53-9, Verapamil	58-64-0, 5'-ADP, biological studies	9002-04-4, Thrombin	65154-06-5, Platelet-activating factor	96426-21-0
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (platelet agonists induce Ca2+ transients in tumor cells by opening receptor-operated channels, effect unrelated to presence of multi-drug resistance phenotype)				
IT	96426-21-0	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (platelet agonists induce Ca2+ transients in tumor cells by opening receptor-operated channels, effect unrelated to presence of multi-drug resistance phenotype)			
RN	96426-21-0	CAPLUS			
CN	L-Serine, glycyl-L-arginylglycyl-L- α -aspartyl- (CA INDEX NAME)				



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 39 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:454320 CAPLUS Full-text

DOCUMENT NUMBER: 129:197698

ORIGINAL REFERENCE NO.: 129:39987a,39990a

TITLE:	Novel chemically modified oligonucleotides provide potent inhibition of P-glycoprotein expression
AUTHOR(S):	Alahari, Suresh K.; Delong, Robert; Fisher, Michael H.; Dean, Nicholas M.; Villet, Pierre; Juliano, R. L.
CORPORATE SOURCE:	Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC, USA
SOURCE:	Journal of Pharmacology and Experimental Therapeutics (1998), 286(1), 419-428

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB One major form of multiple drug resistance (MDR) to cancer therapeutic agents is mediated by overexpression of P-glycoprotein, a membrane ATPase that serves as a drug efflux pump. In humans, this protein is the product of the MDR1 gene. The authors have used chemical modified antisense oligonucleotides to reduce expression of P-glycoprotein in multidrug-resistant fibroblasts and colon carcinoma cells. Although several types of oligonucleotides were tested, compds. having a phosphorothioate backbone and a methoxyethoxy (ME) group at the 2' position of the ribose ring proved to have the greatest potency. Thus, phosphorothioate 2'-ME oligonucleotides directed against either the AUG codon region or the stop codon region of the MDR1 message

produced substantial (50-70%) inhibition of P-glycoprotein expression at concns. of ≤ 50 nM. In addition, such treatment resulted in augmented drug uptake as measured by flow cytometry. Unmodified phosphorothioate compds. of the same sequence were active only in the micromolar range. The authors also tested the ability of several potential delivery agents to enhance the pharmacol. effectiveness of anti-MDR1 oligonucleotides. Both com. Lipofectin, a well known liposomal transfection agent, and a liposomal preparation based on a novel "facial amphiphile" were effective in enhancing their pharmacol. effects of antisense oligonucleotides. A Starburst dendrimer, a type of cationic polymer, was also effective in oligonucleotide delivery. This report emphasizes that significant improvements in antisense pharmacol. can be made through judicious use of both chemical modifications of oligonucleotides and appropriate delivery systems.

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

IT Antitumor agents
Drug delivery systems
Multidrug resistance
Structure-activity relationship
(novel chemical modified antisense oligonucleotides to MDR1 gene provide potent inhibition of P-glycoprotein expression in multidrug-resistant cancer cells in relation to structure and antitumor drug transport and delivery systems)

IT Antitumor agents
(resistance to; novel chemical modified antisense oligonucleotides to MDR1 gene provide potent inhibition of P-glycoprotein expression in multidrug-resistant cancer cells in relation to structure and antitumor drug transport and delivery systems)

IT 107658-43-5 128835-92-7, Lipofectin 211869-94-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel chemical modified antisense oligonucleotides to MDR1 gene provide potent inhibition of P-glycoprotein expression in multidrug-resistant cancer cells in relation to structure and antitumor drug transport and delivery systems)

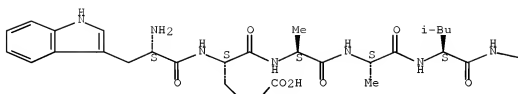
IT 107658-43-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel chemical modified antisense oligonucleotides to MDR1 gene provide potent inhibition of P-glycoprotein expression in multidrug-resistant cancer cells in relation to structure and antitumor drug transport and delivery systems)

RN 107658-43-5 CAPLUS

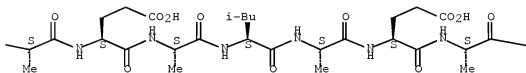
CN L-Alanine, L-tryptophyl-L- α -glutamyl-L-alanyl-L-alanyl-L-leucyl-L-alanyl-L- α -glutamyl-L-alanyl-L-leucyl-L-alanyl-L- α -glutamyl-L-alanyl-L-leucyl-L-histidyl-L-leucyl-L-alanyl-L- α -glutamyl-L-alanyl-L-leucyl-L-alanyl-L- α -glutamyl-L-alanyl-L-leucyl-L- α -glutamyl-L-alanyl-L-leucyl-L-alanyl- (CA INDEX NAME)

Absolute stereochemistry.

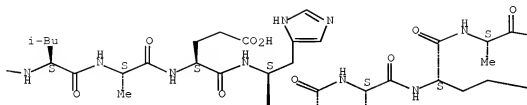
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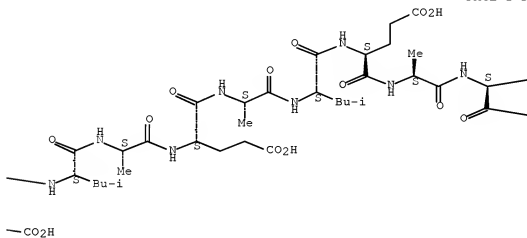
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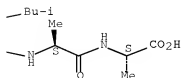
PAGE 1-C



PAGE 1-D

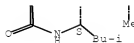


PAGE 1-E



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PAGE 2-C



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 40 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:441458 CAPLUS Full-text

DOCUMENT NUMBER: 129:193578

ORIGINAL REFERENCE NO.: 129:39229a,39232a

TITLE: HPMA copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line

AUTHOR(S): Minko, T.; Kopeckova, P.; Pozharov, V.; Kopecek, J.

CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry/CCCD, University of Utah, Salt Lake City, UT, 84112, USA

SOURCE: Journal of Controlled Release (1998), 54(2), 223-233

CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-(2-Hydroxypropyl)methacrylamide (HPMA) copolymer-adriamycin (ADR) conjugate containing lysosomally degradable oligopeptide (GFLG) side chains terminated in ADR was synthesized. The effect of free and HPMA copolymer-bound ADR on the viability of A2780 sensitive and A2780/AD multidrug resistant human ovarian carcinoma cells was studied in vitro. As expected, the IC50 dose for the HPMA copolymer-ADR conjugate was higher than for free ADR reflecting the difference in the mechanism of cell entry. The resistant A2780/AD cells demonstrated about 40-times higher resistance to free ADR than the sensitive A2780 cells. On the contrary, there was only a small difference in cytotoxicity of the HPMA copolymer-ADR conjugate toward sensitive A2780 or MDR resistant A2780/AD cells. The IC50 value for A2780/AD was only about 20% higher than the value for sensitive A2780 cells. These data seem to indicate that the HPMA copolymer-ADR conjugate may, at least partially, avoid the ATP driven P-glycoprotein (Pgp) efflux pump. The anal. of the expression of the MDR1 gene which encodes the Pgp, has shown that free ADR in high doses stimulated MDR1 gene expression in sensitive A2780 cells. At the same time both free and HPMA copolymer-ADR conjugate partially inhibited the expression of the MDR1 and β 2m genes in multidrug resistant A2780/AD cells.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

IT Ovary, neoplasms

(carcinoma, inhibitors; HPMA copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line)

IT Antitumor agents

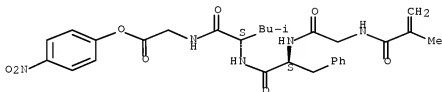
- (ovary carcinoma; HPMa copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line)
- IT Antitumor agents
(resistance to; HPMa copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line)
- IT 25316-40-9DP, Adriamycin, reaction products with HPMa-peptide methacrylate copolymer 100424-72-4DP, reaction products with adriamycin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HPMa copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line)
- IT 100424-72-4DE, reaction products with adriamycin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HPMa copolymer bound adriamycin overcomes MDR1 gene encoded resistance in a human ovarian carcinoma cell line)
- RN 100424-72-4 CAPLUS
- CN Glycine, N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-L-phenylalanyl-L-leucyl-, 4-nitrophenyl ester, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (CA INDEX NAME)

CM 1

CRN 100424-71-3

CMF C29 H35 N5 O8

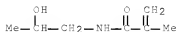
Absolute stereochemistry.



CM 2

CRN 21442-01-3

CMF C7 H13 N O2



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 41 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1998:299936 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 129:89999

ORIGINAL REFERENCE NO.: 129:18371a,18374a

TITLE: Use of the comet test in the evaluation of multidrug resistance of human cell lines

AUTHOR(S): Mattii, L.; Barale, R.; Petrini, M.

CORPORATE SOURCE: UO Ematologia, Università di Pisa, Italy

SOURCE: Leukemia (1998), 12(4), 627-632

CODEN: LEUKED; ISSN: 0887-6924

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The comet test is a reported method for measuring DNA damage in individual mammalian cells. In the present report, the ability of this test to detect multidrug resistance (MDR) was evaluated. For this purpose, two human leukemia, well-characterized parental cell lines, HL60 and CEM, and their derived multidrug-resistant cells, HL60/DNR and CEM/VBL, were cultured with or without different anti-cancer agents. To evaluate the comet test, two DNA-damaging agents were used: daunorubicin (DNR) which is involved in MDR, and ambamustine (AMBA), which is independent from MDR. Moreover, to evaluate the specificity of the comet test, the activity of vinblastine (VBL), an MDR-related, DNA-independent anti-cancer drug, was also tested. Finally, the specificity of the comet test in detecting MDR was confirmed by culturing parental or resistant cells with DNR with or without the revertant agent verapamil (VER). Results confirm that the comet test is able to predict cellular chemoresistance when DNA damaging agents are tested. Finally, expts. on the role of the comet test in evaluating certain aspects of DNA repair are discussed.

CC 1-6 (Pharmacology)

IT Antitumor agents

DNA repair

Multidrug resistance

(comet test in evaluation of multidrug resistance of human cell lines)

IT Antitumor agents

(resistance to; comet test in evaluation of multidrug resistance of human cell lines)

IT 20830-81-3 85754-59-2

RL: EAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(comet test in evaluation of multidrug resistance of human cell lines)

IT 85754-59-2

RL: BAC (Biological activity or effector, except adverse); BSU

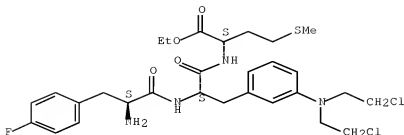
(Biological study, unclassified); BIOL (Biological study)

(comet test in evaluation of multidrug resistance of human cell lines)

RN 85754-59-2 CAPLUS

CN L-Methionine, 4-fluoro-L-phenylalanyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 42 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:140764 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 128:180674

ORIGINAL REFERENCE NO.: 128:35663a

TITLE: Preparation of tryptic digestion-resistant, methylated

lysine-rich lytic peptides by reductive methylation

Julian, Gordon R.; Jaynes, Jesse M.

INVENTOR(S): Demeter Biotechnologies, Ltd., USA

PATENT ASSIGNEE(S): U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 148,889, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5717064	A	19980210	US 1995-427001	19950424 <--
US 6559281	B1	20030506	US 1998-19922	19980206 <--
PRIORITY APPLN. INFO.:			US 1993-148889	B2 19931108 <--
			US 1993-39620	B2 19930604 <--
			US 1993-148491	B2 19931108 <--
			US 1994-225476	B2 19940408 <--
			US 1994-231730	A1 19940420 <--
			US 1995-427001	A3 19950424 <--
			US 1996-689489	A2 19960812 <--

AB A tryptic digestion-resistant, non-naturally occurring lytic peptide comprising a sequence of amino acid residues containing mainly Ala, Val, and Lys amino acid residues, wherein the Lys ϵ -amino groups and the N-terminal amino acid α -amino group are sufficiently methylated to impart enhanced tryptic, chymotryptic, and aminopeptidase digestion resistance to the peptide. The secondary conformation of the peptide is an ordered periodic structure such as an amphipathic α -helix or a β -pleated sheet. The compns. of the invention are suitable for in vivo administration. A method of making the same, to impart enhanced tryptic digestion-resistance thereto, comprising reductively alkylating the Lys ϵ -amino groups and the N-terminal amino acid α -amino group with a methyl-providing reagent in the presence of an heterocyclic amine-borane reducing agent for sufficient time and at sufficient conditions to methylate the α - and ϵ -amino groups to sufficient extent to confer enhanced proteolytic digestion-resistance to the peptide. Thus, lysine-rich peptide H-Phe-Ala-Leu-Ala-Leu-Lys-Ala-Leu- Lys-Lys-Lys-Leu-Lys-Lys-Ala-Leu-Lys-Lys-Ala-Leu-OH (mellitin analog DP-1) in HEPES buffer was treated with pyridine-borane and formaldehyde for 2 h at room temperature to give

essentially complete Lys ϵ -dimethylation and N-terminal dimethylation. The N-methylated products showed biol. activity similar to the unmethylated peptides, but were considerable more stable to trypsin degradation

IC ICM C07K005-00

ICS C07K007-00; C07K017-00; A61K038-00

INCL 530324000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT Antibacterial agents

Antitumor agents

Fungicides

(preparation of tryptic digestion-resistant, methylated lysine-rich lytic peptides by reductive methylation)

IT 162136-46-1DP, N-methylated 162136-47-2DP, N-methylated

162136-48-3DP, N-methylated 162136-49-4DP, N-methylated

162136-54-1DP, N-methylated 162136-59-6DP, N-methylated

162136-60-9DP, N-methylated 162136-61-0DP, N-methylated

162136-62-1DP, N-methylated 162136-64-3DP, N-methylated

162136-65-4DP, N-methylated 162136-66-5DP, N-methylated

162136-67-6DP, N-methylated 162136-69-8DP, N-methylated

162136-70-1DP, N-methylated 162136-71-2DP, N-methylated

162136-72-3DP, N-methylated 162136-73-4DP, N-methylated

162136-74-5DP, N-methylated 162136-75-6DP, N-methylated

162136-76-7DP, N-methylated 166798-61-4DP, N-methylated

166798-62-5DP, N-methylated 170014-06-9DP, N-methylated

170014-07-0DP, N-methylated 170136-47-7DP, N-methylated 170136-48-8DP,

N-methylated 172212-28-1DP, N-methylated 203206-63-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of tryptic digestion-resistant, methylated lysine-rich lytic peptides by reductive methylation)

IT 50-00-0, Formaldehyde, reactions 110-51-0, Pyridine-borane

133084-63-6 162136-77-8 162136-78-9

162136-79-0 170014-11-6 170014-12-7

170014-15-0 176392-57-7 176392-58-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tryptic digestion-resistant, methylated lysine-rich lytic peptides by reductive methylation)

IT 162136-46-1DP, N-methylated 162136-47-2DP, N-methylated

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162136-54-1DP, N-methylated 162136-59-6DP, N-methylated

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172212-28-1DP, N-methylated 203206-63-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

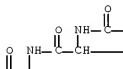
(Uses)

(preparation of tryptic digestion-resistant, methylated lysine-rich lytic peptides by reductive methylation)

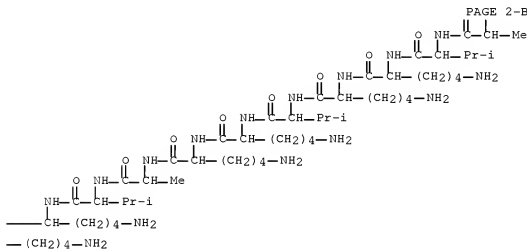
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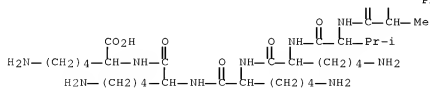
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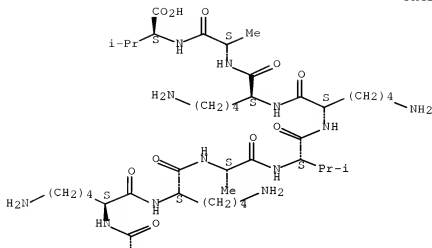
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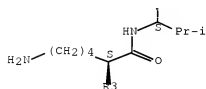
RN 162136-47-2 CAPLUS

CN L-Lysine, L-phenylalanyl-L-alanyl-L-valyl-L-alanyl-L-valyl-L-lysyl-L-alanyl-L-valyl-L-alanyl-L-valyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-

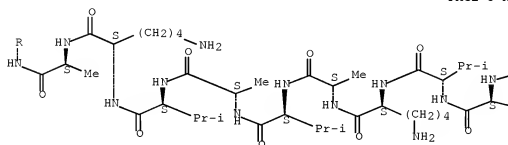
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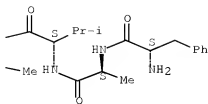
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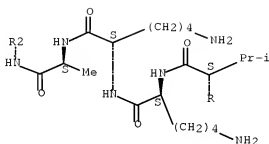
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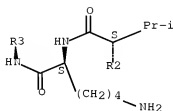
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PAGE 4-A



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RN 162136-54-1 CAPLUS

CN L-Phenylalanine, L-alanyl-L-valyl-L-lysyl-L-arginyl-L-valylglycyl-L-arginyl-L-arginyl-L-leucyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-L-arginyl-L-lysyl-L-isoleucyl-L-alanyl-L-arginyl-L-leucylglycyl-L-valyl-L-alanyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

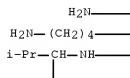
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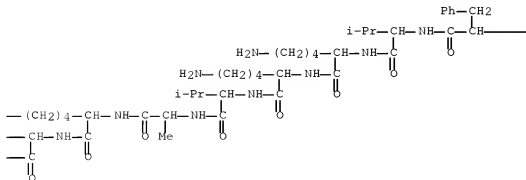
RN 162136-59-6 CAPLUS

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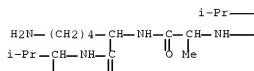
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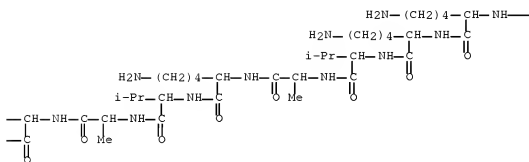
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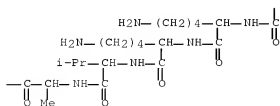
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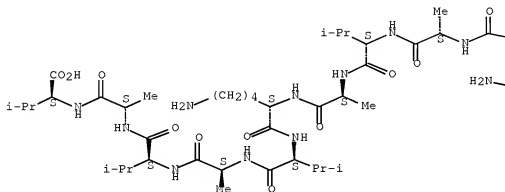


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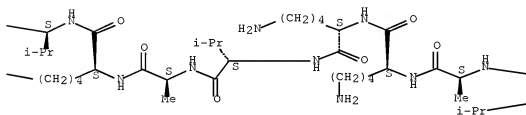
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Absolute stereochemistry.

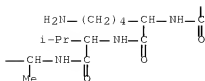
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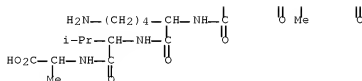
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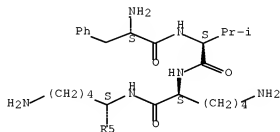


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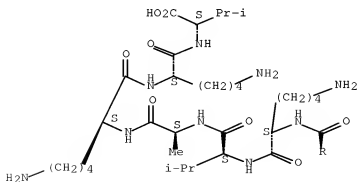
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Absolute stereochemistry.

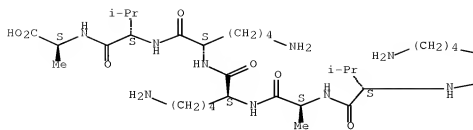
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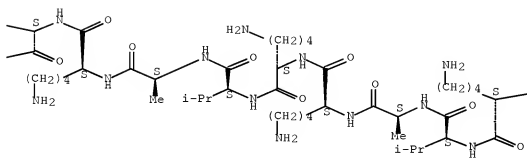
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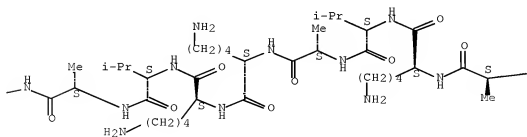
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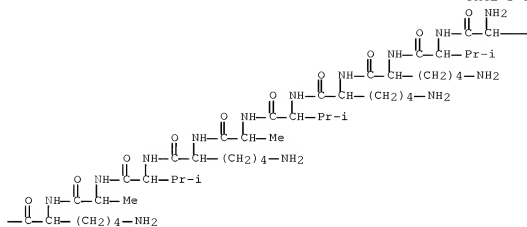
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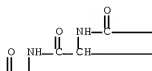
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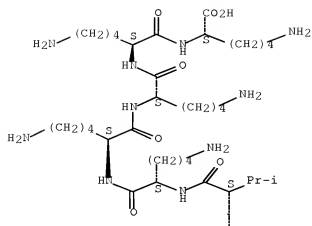
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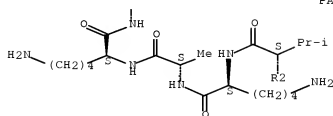
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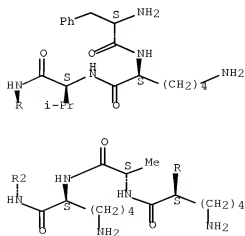
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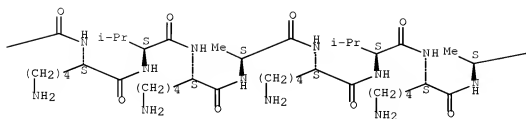
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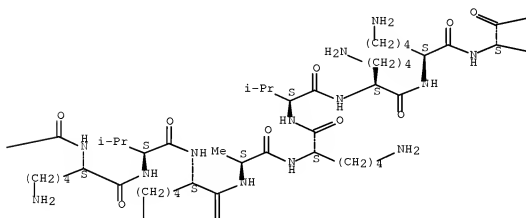
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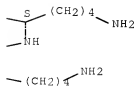
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PAGE 1-C

HO₂C

PAGE 1-D



PAGE 2-C

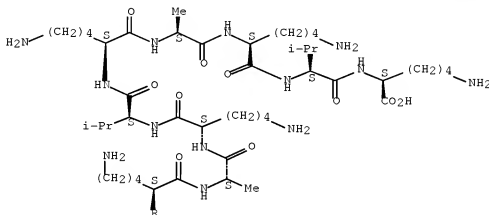


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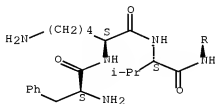
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Absolute stereochemistry.

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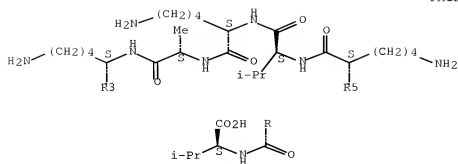


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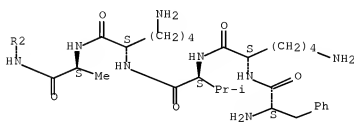
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Absolute stereochemistry.

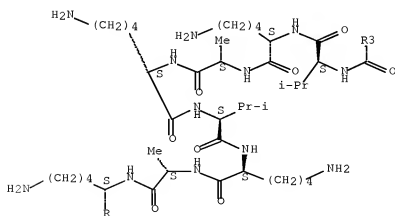
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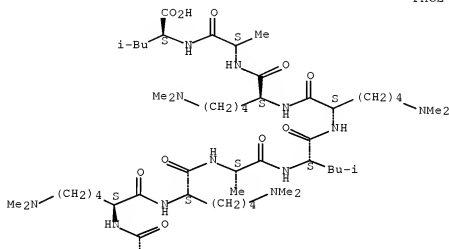


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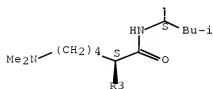
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Absolute stereochemistry.

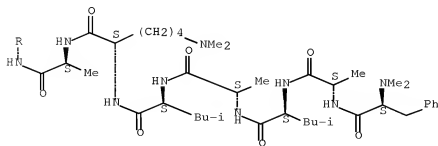
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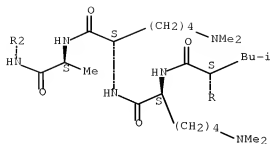
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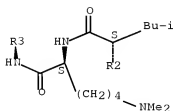
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IT 133084-63-6 162136-77-8 162136-78-9
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RL: RCT (Reactant); RACT (Reactant or reagent)

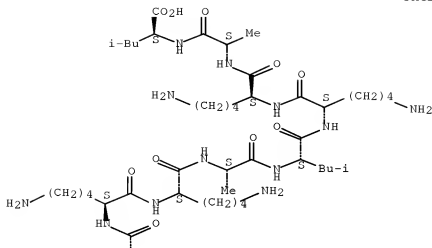
(preparation of tryptic digestion-resistant, methylated lysine-rich lytic peptides by reductive methylation)

RN 133084-63-6 CAPLUS

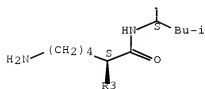
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Absolute stereochemistry.

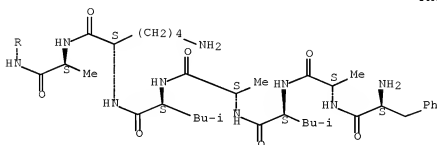
PAGE 1-A



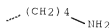
PAGE 2-A



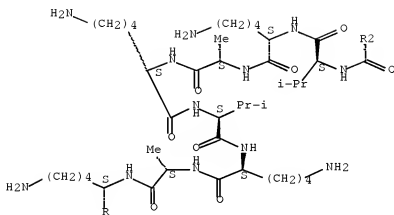
PAGE 3-A



PAGE 1-B



PAGE 2-A

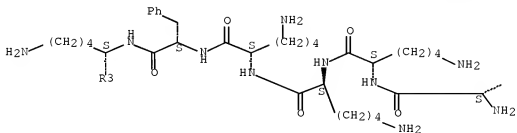


RN 162136-78-9 CAPLUS

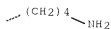
CN L-Alanine, L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-phenylalanyl-L-lysyl-L-valyl-L-lysyl-L-alanyl-L-lysyl-L-valyl-L-lysyl-L-alanyl-L-lysyl-L-valyl-L-lysyl-L-alanyl-L-lysyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

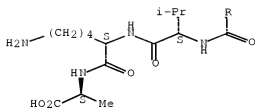
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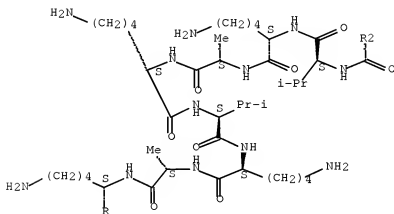
PAGE 1-B



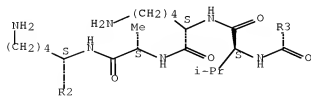
PAGE 2-A



PAGE 3-A



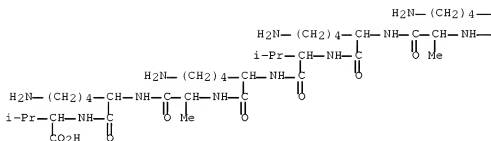
PAGE 4-A



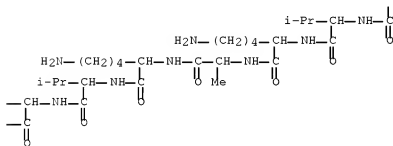
RN 162136-79-0 CAPLUS

CN L-Valine, L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-phenylalanyl-L-lysyl-L-valyl-L-

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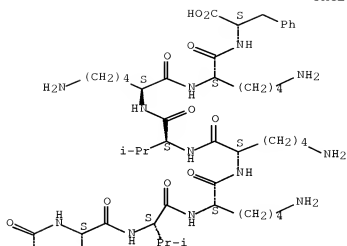


RN 170014-11-6 CAPLUS

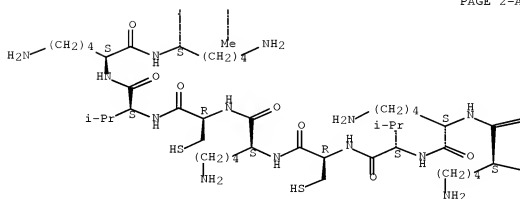
CN L-Phenylalanine, L-phenylalanyl-L-lysyl-L-lysyl-L-valyl-L-lysyl-L-lysyl-L-
valyl-L-alanyl-L-lysyl-L-lysyl-L-valyl-L-cysteinyl-L-lysyl-L-cysteinyl-L-
valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-valyl-L-lysyl-L-
lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

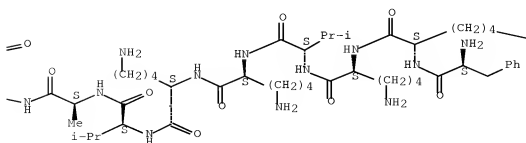
PAGE 1-A



PAGE 2-A



PAGE 2-B



PAGE 2-C

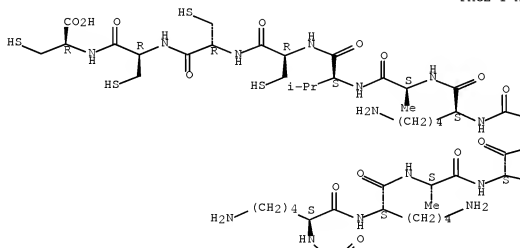


RN 170014-12-7 CAPLUS

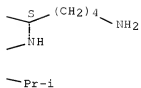
CN L-Cysteine, L-phenylalanyl-L-alanyl-L-valyl-L-alanyl-L-valyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-cysteinyl-L-cysteinyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

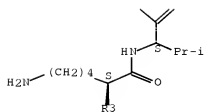
PAGE 1-A



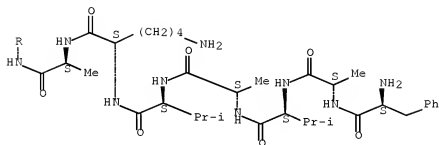
PAGE 1-B



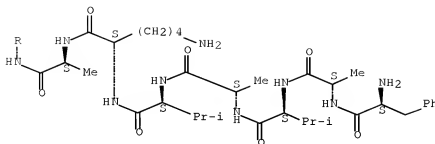
PAGE 2-A



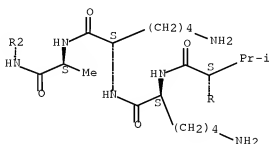
PAGE 3-A



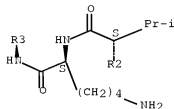
PAGE 3-A



PAGE 4-A



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REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 43 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:548822 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 127:229188

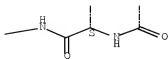
ORIGINAL REFERENCE NO.: 127:44527a,44530a

TITLE: An N-myristoylated protein kinase C- α pseudosubstrate peptide that functions as a multidrug resistance reversal agent in human breast cancer cells is not a P-glycoprotein substrate
 AUTHOR(S): Bergman, Philip J.; Gravitt, Karen R.; O'Brian, Catherine A.

CORPORATE SOURCE: Anderson Cancer Center, University Texas, Houston, TX,
77030, USA
SOURCE: Cancer Chemotherapy and Pharmacology (1997),
40(5), 453-456
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

- AB Protein kinase C- α (PKC- α) activation is an important contributing factor in human breast cancer MCF-7 MDR cell drug resistance. It was recently reported the use of N-myristoylated PKC- α pseudosubstrate peptides with potent PKC- α inhibitory activity as reversal agents of drug resistance in MCF-7 MDR cells. The peptides potentially inhibit phosphorylation of the PKC- α substrates P-glycoprotein (P-gp), raf kinase, and PKC- α itself in MCF-7 MDR cells in association with a severalfold induction of intra-cellular uptake of P-gp substrate chemotherapeutics and a 2-fold increase in cellular chemosensitivity. It is reported now that the N-myristoylated PKC- α pseudosubstrate peptide N-myristoyl-RFARKGALRQKNV (P3) is not a P-gp substrate in MCF-7 MDR cells based on a comparison of the cellular uptake of [125I]-radiolabeled P3 in MCF-7 MDR vs MCF-7 WT cells. The extent of cellular uptake of the radiolabeled peptide in the drug-resistant cell line MCF-7 MDR was either greater than or equivalent to the uptake in the parental drug-sensitive MCF-7 WT cell line over a time course of 30 min to 6 h, and across a peptide concentration range of 25-100 μ M. Addnl., treatment of the MCF-7 MDR cells with verapamil (VPL), a known P-gp efflux inhibitor, had no effect on the cellular accumulation of radiolabeled P3. The results provide direct evidence that the N-myristoylated pseudosubstrate peptide is taken up equivalently by drug-sensitive and MDR cancer cells and therefore has potential value as an MDR reversal agent that operates by a novel mechanism.
- CC 1-2 (Pharmacology)
- IT Antitumor agents
(N-myristoylated protein kinase C- α pseudosubstrate peptide functions as a multidrug resistance reversal agent)
- IT 169305-85-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(N-myristoylated protein kinase C- α pseudosubstrate peptide functions as a multidrug resistance reversal agent)
- IT 169305-85-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(N-myristoylated protein kinase C- α pseudosubstrate peptide functions as a multidrug resistance reversal agent)
- RN 169305-85-5 CAPLUS
- CN L-Valine, N2-(1-oxotetradecyl)-L-arginyl-L-phenylalanyl-L-alanyl-L-arginyl-L-lysylglycyl-L-alanyl-L-leucyl-L-leucyl-L-glutamyl-L-lysyl-L-asparaginy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 44 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1997:185126 CAPLUS Full-text
 DOCUMENT NUMBER: 126:235368
 ORIGINAL REFERENCE NO.: 126:45481a,45484a
 TITLE: Biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compositions, and compound preparation and characterization
 INVENTOR(S): Axworthy, Donald B.; Theodore, Louis J.; Gustavson, Linda M.; Reno, John M.
 PATENT ASSIGNEE(S): Neorx Corp., USA
 SOURCE: U.S., 79 pp., Cont.-in-part of U.S. Ser. No. 995,383, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 14
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5608060	A	19970304	US 1995-351469	19950221 <--
US 5283342	A	19940201	US 1992-895588	19920609 <--
WO 9325240	A2	19931223	WO 1993-US5406	19930607 <--
WO 9325240	A3	19940217		
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1138334	A2	20011004	EP 2001-201994	19930607 <--
EP 1138334	A3	20020403		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5911969	A	19990615	US 1994-329617	19941026 <--
US 5955605	A	19990921	US 1996-695940	19960812 <--
PRIORITY APPLN. INFO.:			US 1992-895588	A2 19920609 <--
			US 1992-995381	B2 19921223 <--
			US 1992-995383	B2 19921223 <--
			WO 1993-US5406	W 19930607 <--
			EP 1993-915235	A3 19930607 <--
			US 1995-351469	A3 19950221 <--

OTHER SOURCE(S): MARPAT 126:235368

AB Biotinidase-resistant biotin-DOTA conjugates, and methods of use thereof in diagnostic and therapeutic pretargeting methods are provided. These conjugates are useful in diagnosis and treatment of cancer. The invention relates to methods, compds., compns. and kits useful for delivering, to a target site, a targeting moiety that is conjugated to one member of a ligand/anti-ligand pair. After localization and clearance of the targeting moiety conjugate, direct or indirect binding of a diagnostic or therapeutic agent conjugate at the target site occurs. Methods for radiometal labeling of biotin and for improved radiohalogenation of biotin, as well as the related compds., are also disclosed. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention-enhancing moieties, and addnl. methods are set forth.

IC ICM C07D257-02
 ICS C07D495-04; A61K031-415; C07H017-04
 INCL 540474000
 CC 8-9 (Radiation Biochemistry)
 Section cross-reference(s): 26, 28, 63, 78
 IT Antitumor agents
 Neoplasm
 (biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)
 IT Intestine, neoplasm
 (colon, carcinoma; biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)
 IT 58-85-5D, Biotin, DOTA conjugates 10098-91-6D, Y 90, complexes with biotinyl-DOTA derivative, biological studies 14133-76-7D, Tc-99, complexes with chelate-biotin conjugate, biological studies 14265-75-9D, complexes with biotinyl-DOTA derivative, biological studies 14998-63-1D, Re-186, complexes with chelate-biotin conjugate, biological studies 60239-18-1D, DOTA, biotin conjugates 154024-46-1D, Tc-99 and Re-186 complexes 154024-49-4 188428-77-5 188428-78-6 188428-79-7 188428-80-0 188428-81-1 188428-82-2
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)
 IT 1926-80-3P, Methyl 6-aminocaproate hydrochloride 14273-90-6P, Methyl 6-bromocaproate 68617-64-1P, 3-(2-Pyridinyldithio)propanoic acid 115616-51-8P 154024-46-1P 154024-51-8P 154024-52-9P 154024-53-0P, 2'-Dehydroxroridin A 154024-55-2P 154024-56-3P 154024-57-4P 154024-60-9P 154024-64-3P 154024-65-4P 154024-67-6P 154024-68-7P 154024-69-8P 154024-72-3P, Biotinyl-D-alanine 154024-74-5P 154024-75-6P 154024-76-7P, (N-Methyl)glycylbiotin 154073-73-1P 154073-74-2P 167861-65-6P 168404-98-6P 168404-99-7P 168405-00-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction; biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)
 IT 60-32-2, 6-Aminocaproic acid 107-96-0 107-97-1, N-Methylglycine 108-24-7, Acetic anhydride 338-69-2, D-Alanine 407-25-0, Trifluoroacetic anhydride 576-19-2 2269-44-5 2637-34-5, 2-Mercaptopyridine 4224-70-8, 6-Bromocaproic acid 6066-82-6, N-Hydroxysuccinimide 9004-54-0D, Dextran, biotinylated, reactions 9013-20-1D, Streptavidin, SMCC reaction products 10387-40-3, Potassium thioacetate 14729-29-4, Roridin A 18162-48-6, tert-Butyldimethylsilyl chloride 23288-60-0 35013-72-0 64987-85-5D, SMCC, reaction products with avidin and streptavidin 72040-64-3 87552-16-7 115416-38-1 123317-52-2 125215-72-7 154024-45-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)
 IT 154024-46-1D, Tc-99 and Re-186 complexes
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

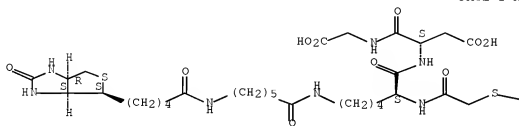
(biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)

RN 154024-46-1 CAPLUS

CN Glycine, N6-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-N2-[[[(tetrahydro-2H-pyran-2-yl)thio]acetyl]-L-lysyl-L- α -aspartyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction; biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compd. prepn. and characterization)

IT 154024-45-0

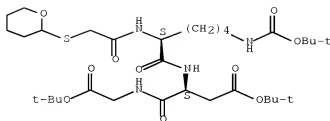
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; biotinidase-resistant biotin-DOTA conjugates for treatment and diagnosis of cancer, (pre)targeting procedures and compns., and compound preparation and characterization)

RN 154024-45-0 CAPLUS

CN Glycine, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[[[(tetrahydro-2H-pyran-2-yl)thio]acetyl]-L-lysyl-L- α -aspartyl-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 45 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:386247 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 125:56243

ORIGINAL REFERENCE NO.: 125:10837a,10840a

TITLE: Polyclonal antibody to multidrug resistance-associated protein

INVENTOR(S): Akyama, Shinichi; Sumizawa, Tomoyuki; Takenaga, Sanae

PATENT ASSIGNEE(S): Nichirei Kk, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

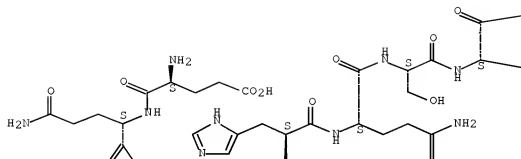
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

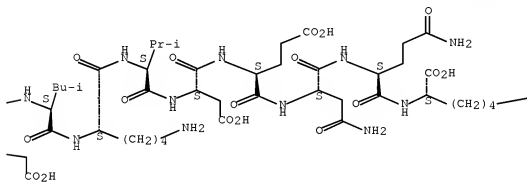
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 08113600	A	19960507	JP 1994-273075	19941013 <--
PRIORITY APPLN. INFO.:				JP 1994-273075	19941013 <--
AB	Disclosed is a polyclonal antibody useful for early detection of tumor with multidrug resistance-associated protein (MRP). Polyclonal anti-MRP antibody was prepared by immunizing rabbit with peptide of sequence Glu-Gln-Glu-Arg-Phe-Ile-His-Gln-Ser-Asp-Leu-Lys-Val-Asp-Glu-Asn-Gln-Lys.				
IC	ICM C07K016-32				
ICA	ICS G01N033-53; G01N033-574				
ICA	A61K039-395				
CC	15-3 (Immunochemistry)				
IT	Neoplasm				
	(multidrug-resistant; polyclonal antibody to multidrug resistance-associated protein)				
IT	178119-40-9				
	RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(polyclonal antibody to multidrug resistance-associated protein)				
IT	178119-40-9				
	RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(polyclonal antibody to multidrug resistance-associated protein)				
RN	178119-40-9 CAPLUS				
CN	L-Lysine, L- α -glutamyl-L-glutamyl-L- α -glutamyl-L-arginyl-L-phenylalanyl-L-isoleucyl-L-histidyl-L-glutamyl-L-seryl-L- α -aspartyl-L-leucyl-L-lysyl-L-valyl-L- α -aspartyl-L- α -glutamyl-L-asparaginyl-L-glutamyl- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.

PAGE 1-A

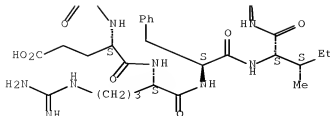


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L80 ANSWER 46 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1995:907682 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 123:340967
 ORIGINAL REFERENCE NO.: 123:61223a,61226a
 TITLE: Preparation of digestion-resistant methylated
 lysine-rich lytic peptides as drugs.
 INVENTOR(S): Julian, Gordon R.
 PATENT ASSIGNEE(S): Demeter Biotechnologies Ltd., USA
 SOURCE: PCT Int. Appl., 66 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 11
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513085	A1	19950518	WO 1994-US12550	19941101 <--
W: AU, CA, FI, JP, KR, NO, NZ				
RU: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9510865	A	19950529	AU 1995-10865	19941101 <--
PRIORITY APPLN. INFO.:			US 1993-148889	A 19931108 <--
			WO 1994-US12550	W 19941101 <--

AB Tryptic digestion-resistant, non-naturally occurring lytic peptides containing mainly Ala, Val, and Lys, wherein the ϵ -amino groups of the Lys residues and the α -amino group of the N-terminal amino acid are methylated were prepared. The secondary conformation of the peptide is an ordered periodic structure such as an amphipathic α -helix or a β -pleated sheet. Thus, H-Phe-Ala-Leu-Ala-Leu-Lys-Ala-Leu-Lys-Lys-Ala-Leu-Lys-Lys-Ala-Leu-Lys-Lys-Ala-Leu-OH (mellitin analog DP-1) in HEPES buffer was treated with pyridine.borane and H2CO for 2 h at room temperature to give essentially complete methylation. The product was active against *Pseudomonas aeruginosa* at 10 μ M but not at 1 μ M.

IC ICM A61K038-00
 ICS C07K005-00; C07K007-00; C07K017-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1

IT Bactericides, Disinfectants, and Antiseptics
 Fungicides and Fungistats
 Neoplasm inhibitors
 Protozoacides
 Virucides and Virustats
 (preparation of digestion-resistant methylated lysine-rich lytic peptides as drugs)

IT 162136-46-1DP, N-methylated 162136-47-2DP, N-methylated

162136-46-3DP, N-methylated 162136-49-4DP, N-methylated
 162136-50-7DP, N-methylated 162136-59-6DP, N-methylated
 162136-60-9DP, N-methylated 162136-61-6DP, N-methylated
 162136-62-1DP, N-methylated 162136-64-3DP, N-methylated
 162136-65-4DP, N-methylated 162136-66-5DP, N-methylated
 162136-67-6DP, N-methylated 162136-69-8DP, N-methylated
 162136-70-1DP, N-methylated 162136-74-5DP, N-methylated
 162136-75-6DP, N-methylated 162136-76-7DP, N-methylated
 162136-77-8DP, N-methylated 162136-78-9DP, N-methylated
 162136-79-0DP, N-methylated 166798-61-4DP, N-methylated
 166798-62-5DP, N-methylated 170014-06-9DP, N-methylated
 170014-07-0DP, N-methylated 170014-08-1DP, N-methylated
 170014-09-2DP, N-methylated 170014-10-5DP, N-methylated
 170014-11-6DP, N-methylated 170014-12-7DP, N-methylated
 170014-13-8DP, N-methylated 170014-14-9DP, N-methylated
 170014-15-0DP, N-methylated 170136-47-7DP, N-methylated
 170136-48-8DP, N-methylated

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of digestion-resistant methylated lysine-rich lytic
 peptides as drugs)

IT 123084-63-6

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of digestion-resistant methylated lysine-rich lytic peptides
 as drugs)

IT 162136-46-1DP, N-methylated 162136-47-2DP, N-methylated
 162136-48-3DP, N-methylated 162136-49-4DP, N-methylated
 162136-50-7DP, N-methylated 162136-59-6DP, N-methylated
 162136-60-9DP, N-methylated 162136-61-6DP, N-methylated
 162136-62-1DP, N-methylated 162136-64-3DP, N-methylated
 162136-65-4DP, N-methylated 162136-66-5DP, N-methylated
 162136-67-6DP, N-methylated 162136-69-8DP, N-methylated
 162136-70-1DP, N-methylated 162136-74-5DP, N-methylated
 162136-75-6DP, N-methylated 162136-76-7DP, N-methylated
 162136-77-8DP, N-methylated 162136-78-9DP, N-methylated
 162136-79-0DP, N-methylated 170014-06-9DP, N-methylated
 170014-08-1DP, N-methylated 170014-09-2DP, N-methylated
 170014-10-5DP, N-methylated 170014-11-6DP, N-methylated
 170014-12-7DP, N-methylated 170014-13-8DP, N-methylated
 170014-14-9DP, N-methylated 170014-15-0DP, N-methylated

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

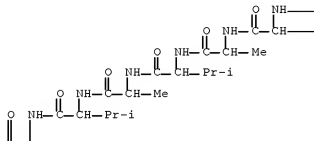
(preparation of digestion-resistant methylated lysine-rich lytic
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RN 162136-46-1

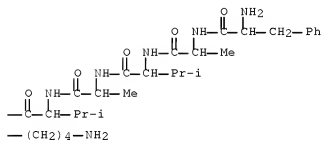
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 lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-
 lysyl-L-lysyl- (9CI) (CA INDEX NAME)

lysyl-L-lysyl-L-alanyl-L-valyl-L-lysyl-L-lysyl-L-lysyl- (9CI) (CA INDEX
NAME)

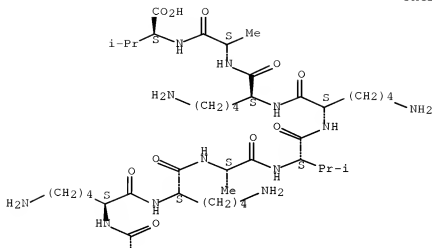
PAGE 1-C



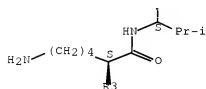
PAGE 1-D



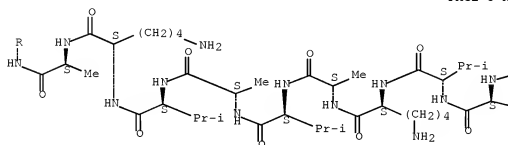
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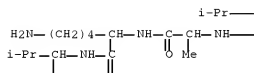
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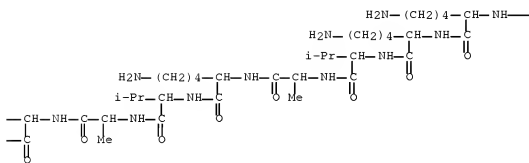
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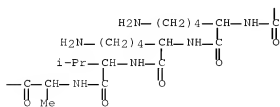
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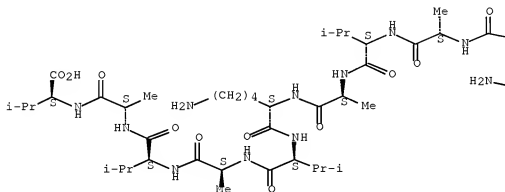


RN 162136-62-1 CAPLUS

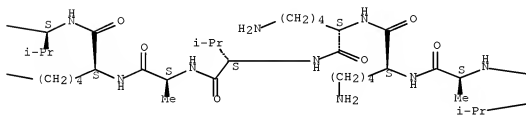
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Absolute stereochemistry.

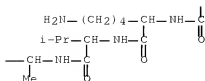
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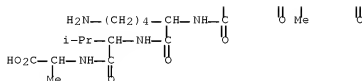
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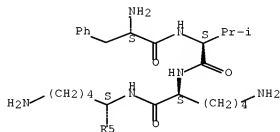


RN 162136-66-5 CAPLUS

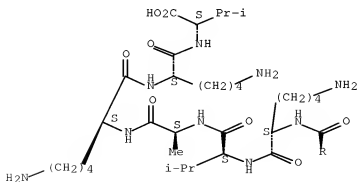
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Absolute stereochemistry.

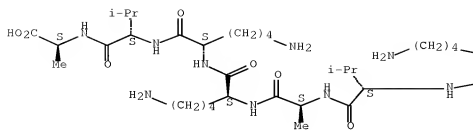
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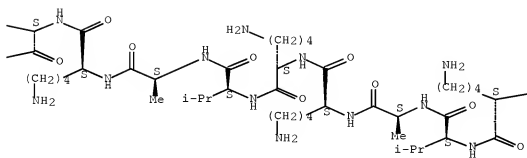
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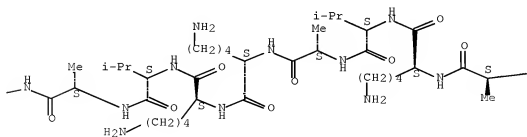
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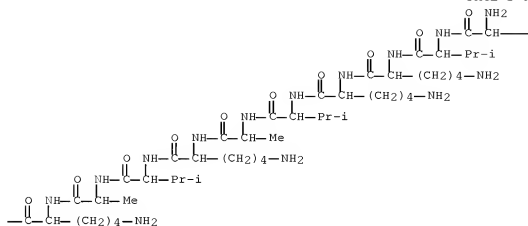
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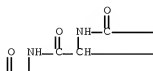
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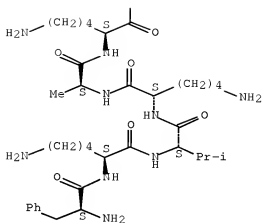
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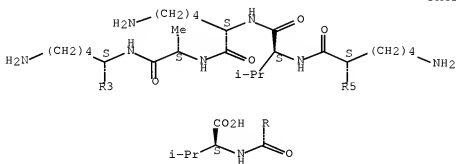


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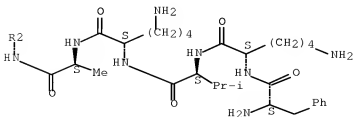
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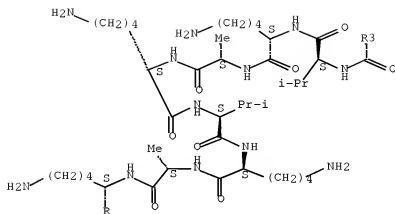
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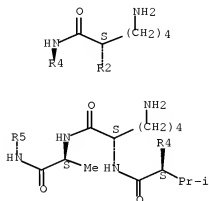
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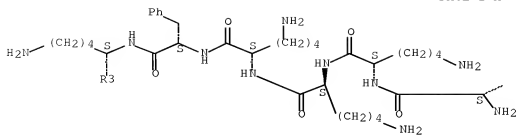


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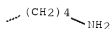
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(CA INDEX NAME)

Absolute stereochemistry.

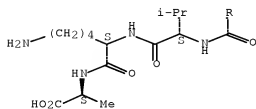
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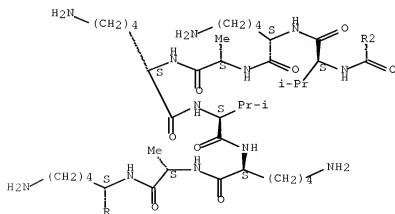
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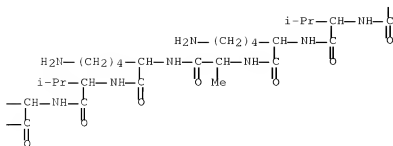
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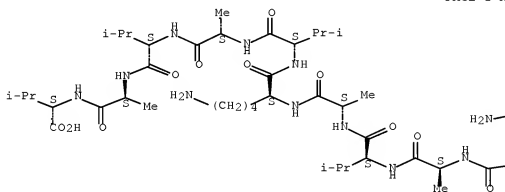


RN 170014-06-9 CAPLUS

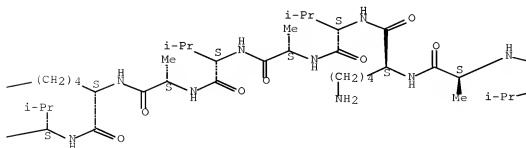
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Absolute stereochemistry.

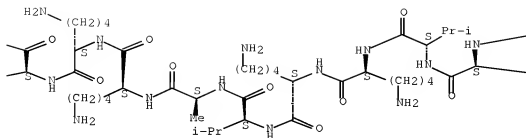
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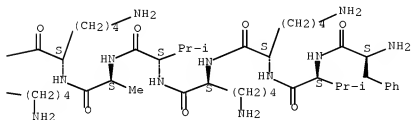
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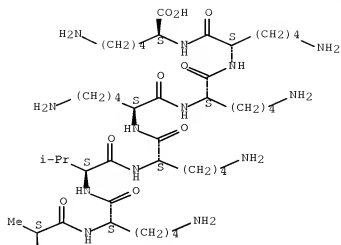


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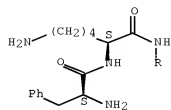
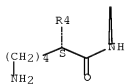
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Absolute stereochemistry.

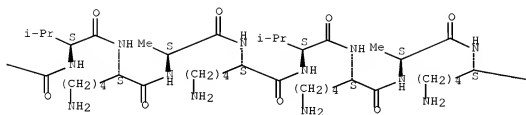
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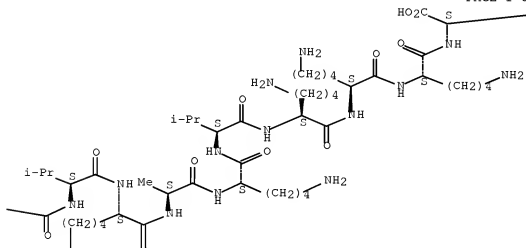
PAGE 2-A



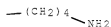
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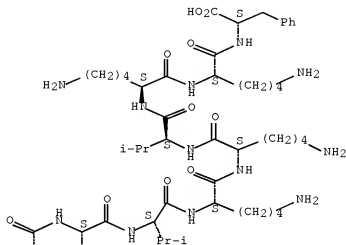


RN 170014-11-6 CAPLUS

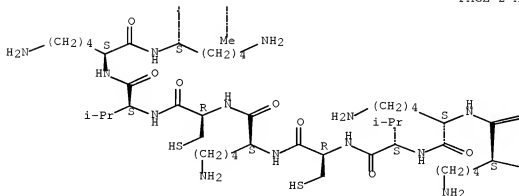
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Absolute stereochemistry.

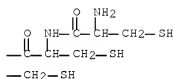
PAGE 1-A



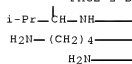
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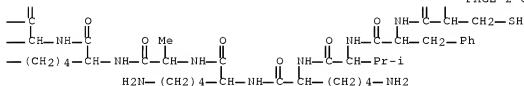
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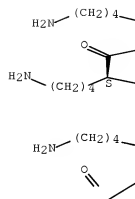


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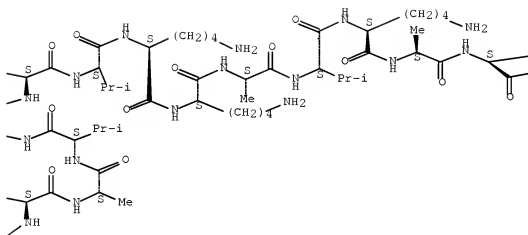
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Absolute stereochemistry.

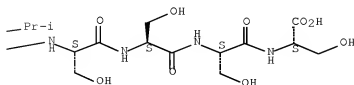
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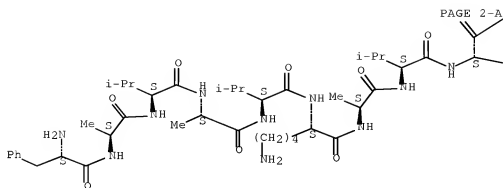


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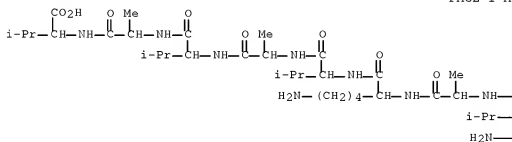
PAGE 2-B



RN 170014-15-0 CAPLUS

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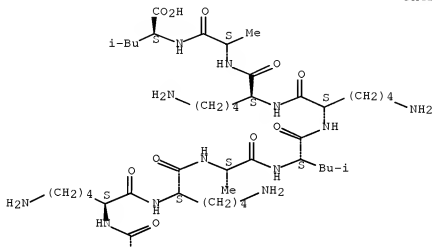


RN 133084-63-6 CAPLUS

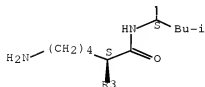
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Absolute stereochemistry.

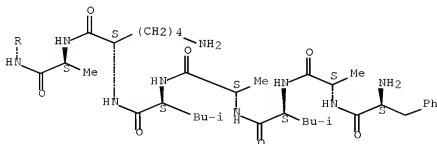
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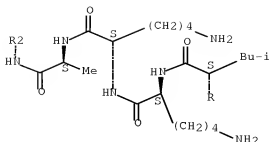
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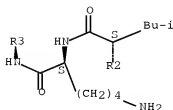
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L80 ANSWER 47 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:809686 CAPLUS Full-text

DOCUMENT NUMBER: 123:311739

ORIGINAL REFERENCE NO.: 123:55839a,55842a

TITLE: Clinical significance of serum concentration of tartrate resistant acid phosphatase

AUTHOR(S): Meng, Xunwu; Xing, Xiaoping; Chen, Li; Liu, Shuqin; Zhou, Xueying; Lu, Zhaolin; Liu, Huichen; Yu, Wei; Shen, Victor W.; Lindsay, Robert

CORPORATE SOURCE: Dep. Endocrinology, Beijing Union Hospital, Beijing, 100730, Peop. Rep. China

SOURCE: Zhonghua Neifenmi Daixie Zazhi (1995), 11(1), 9-11

CODEN: ZNDZEK; ISSN: 1000-6699

PUBLISHER: Shanghaishi Neifenmi Yanjiuso

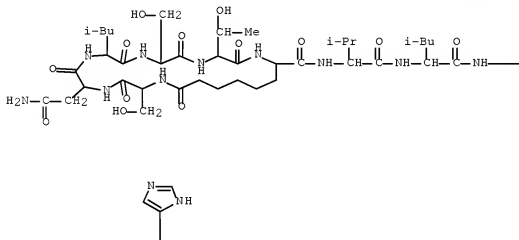
DOCUMENT TYPE: Journal

LANGUAGE: Chinese

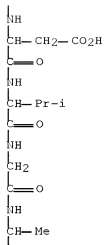
AB The concns. of serum tartrate-resistant acid phosphatase (STr-Acp) were detected in 167 normals and 211 patients with seven different kinds of disease. They were significantly high in the increased bone resorption disease, namely hyperparathyroidism, Paget disease, renal tubular acidosis, metastatic cancer of bone, Cushing syndrome and primary osteoporosis. The concentration was markedly low in the decreased bone resorption disease, i.e. hypoparathyroidism. In the patients with hyperparathyroidism or Paget disease, STr-Acp exhibited a pos. correlation with serum alkaline phosphatase and urinary hydroxyproline excretion. A neg. correlation between STr-Acp and bone mineral d. (BMD) was found in osteoporotic patients with vertebral compression fractures. The levels of STr-Acp decreased significantly in 43 osteoporotic patients treated with elcatonin and 11 cases of hyperparathyroidism after operation.

CC 14-15 (Mammalian Pathological Biochemistry)
 IT Bone, neoplasm
 (metastasis, tartrate resistant acid phosphatase of human serum
 significance in various diseases)
 IT 60731-46-6, Elcatonin
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (tartrate resistant acid phosphatase of human serum
 significance in various diseases and elcatonin therapy)
 IT 60731-46-6, Elcatonin
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (tartrate resistant acid phosphatase of human serum
 significance in various diseases and elcatonin therapy)
 RN 60731-46-6 CAPLUS
 CN 1,7-Dicarbaccalcitonin (eel), 1-butanolic acid- (9CI) (CA INDEX NAME)

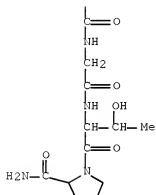
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L80 ANSWER 48 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:561573 CAPLUS Full-text

DOCUMENT NUMBER: 122:299107

ORIGINAL REFERENCE NO.: 122:54328h,54329a

TITLE: Compositions of gastric acid-resistant microspheres containing buffered bile acids

INVENTOR(S): Sipos, Tibor

PATENT ASSIGNEE(S): Digestive Care Inc., USA

SOURCE: U.S., 10 pp. Cont.-in-part of U.S. 5,262,172.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5405621 A 19950411 US 1993-139263 19931110 <--
 US 5262172 A 19931116 US 1992-901749 19920619 <--
 PRIORITY APPLN. INFO.: US 1992-901749 A2 19920619 <--

AB Disclosed are gastric acid-resistant polymer-coated buffered bile acid compns., process for their preps. and methods of treating digestive disorders, impaired liver function, autoimmune diseases of the liver and biliary tract, preventing colon cancer, cholestasis associated with cystic fibrosis, dissolving gallstones and regulating dietary cholesterol absorption by administering the compns. to a mammal in need of such treatment. For example, microspheres were manufactured from a composition containing disintegrant 6.0, buffered 3 α ,7 β -dihydroxy-5 β -cholanolic acid 80.0, anhydrous buffering agent 11.0, and adhesive polymers 3.0%.

IC ICM A61K009-54
 ICS A61K009-58; A61K009-62; A61K009-16

INCL 424490000

CC 63-6 (Pharmaceuticals)

IT Neoplasm inhibitors
 (colon, gastric acid-resistant oral compns. containing buffered bile acids for treatment of bile acid deficiency)

IT Intestine, neoplasm
 (colon, inhibitors, gastric acid-resistant oral compns. containing buffered bile acids for treatment of bile acid deficiency)

IT 56-40-6, Glycine, biological studies 77-86-1, Tromethamine 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 102-71-6, Triethanolamine, biological studies 109-89-7, Diethylamine, biological studies 128-13-2, Ursodeoxycholic acid 128-13-2D, Ursodeoxycholic acid, glycyl derivs. 144-55-8, Sodium bicarbonate, biological studies 474-25-9, Chenodeoxycholic acid 497-19-8, Sodium carbonate, biological studies 506-87-6, Ammonium carbonate 584-08-7, Potassium carbonate 6418-87-7, Triarginine 9003-39-8, PVP 9004-34-6, Cellulose, biological studies 9004-38-0, Cellulose acetate phthalate 9004-64-2, Hydroxypropyl cellulose 9004-67-5, Methyl cellulose 9005-25-8, Starch, biological studies 9005-37-2, Propylene glycol alginate 13184-13-9, Dilysine 13184-14-0, Trilysine 14605-22-2, Tauroursodeoxycholic acid 15483-27-9 24937-47-1, Polyarginine 25104-18-1, Polylysine 25212-18-4, Polyarginine 38000-06-5, Polylysine 130674-38-3

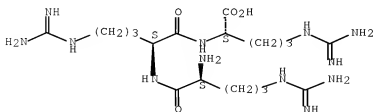
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gastric acid-resistant oral compns. containing buffered bile acids for treatment of bile acid deficiency)

IT 6418-87-7, Triarginine 13184-14-0, Trilysine
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gastric acid-resistant oral compns. containing buffered bile acids for treatment of bile acid deficiency)

RN 6418-87-7 CAPLUS

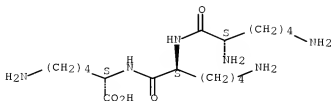
CN L-Arginine, L-arginyl-L-arginyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 13184-14-0 CAPLUS
 CN L-Lysine, L-lysyl-L-lysyl- (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 49 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:320403 CAPLUS Full-text

DOCUMENT NUMBER: 122:150990

ORIGINAL REFERENCE NO.: 122:27677a,27680a

TITLE: Inhibition of protein kinase C by a synthetic peptide corresponding to cytoplasmic domain residues 828 - 848 of the human immunodeficiency virus type 1 envelope glycoprotein

AUTHOR(S): Ward, Nancy E.; Gravitt, Karen R.; O'Brian, Catherine A.

CORPORATE SOURCE: Department of Cell Biology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Box 173, Houston, TX, 77030, USA

SOURCE: Cancer Letters (Shannon, Ireland) (1995), 88(1), 37-40

CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This report describes the inhibition of protein kinase C (PKC) by a synthetic peptide corresponding to a viral sequence expressed in mammalian cells. The peptide corresponds to cytoplasmic domain residues 828-848 of the human immunodeficiency virus type 1 (HIV-1) envelope glycoprotein (gp41), and it inhibits Ca²⁺- and phosphatidylserine (PS)-dependent phosphorylation of synthetic peptide substrates and histone by purified PKC with IC₅₀ values ranging from 9 to 32 μM. Although previously described PKC-inhibitory synthetic peptides corresponding to sequences expressed in mammalian cells are also effective against the phosphorylation of synthetic peptide substrates, they fail to affect PKC-catalyzed phosphorylation of potent protein substrates such as histone. This may limit their usefulness as inhibitors of PKC-catalyzed protein phosphorylation in cellular systems. PKC activation is a major contributing factor in multidrug resistance (MDR) in cancer. The authors observation that the synthetic peptide gp41(828-848) inhibits PKC-catalyzed phosphorylation of a protein substrate suggests the potential value of expressing the viral sequence gp41(828-848) in cancer cells as a novel in vitro model system of MDR reversal.

CC 1-6 (Pharmacology)

IT H₂oplasm inhibitors

(inhibition of protein kinase C by a synthetic peptide corresponding to cytoplasmic domain residues 828-848 of the human immunodeficiency virus type 1 envelope glycoprotein in relation to multidrug resistance reversal in cancer)

IT 148749-31-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); TH9 (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of protein kinase C by a synthetic peptide corresponding to cytoplasmic domain residues 828-848 of the human immunodeficiency virus type 1 envelope glycoprotein in relation to multidrug resistance reversal in cancer)

IT 148749-31-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); TH9 (Therapeutic use); BIOL (Biological study); USES (Uses)

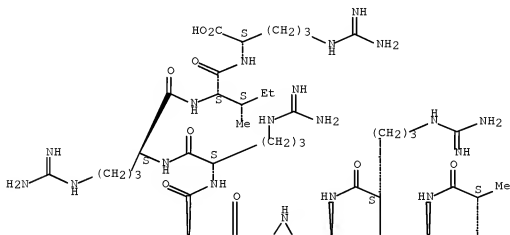
(inhibition of protein kinase C by a synthetic peptide corresponding to cytoplasmic domain residues 828-848 of the human immunodeficiency virus type 1 envelope glycoprotein in relation to multidrug resistance reversal in cancer)

RN 148749-31-9 CAPLUS

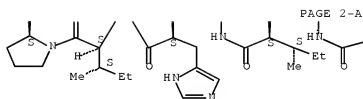
CN L-Arginine, L-arginyl-L-valyl-L-isoleucyl-L- α -glutamyl-L-valyl-L-valyl-L-glutamylglycyl-L-alanyl-L-cysteinyl-L-arginyl-L-alanyl-L-isoleucyl-L-arginyl-L-histidyl-L-isoleucyl-L-prolyl-L-arginyl-L-arginyl-L-isoleucyl- (CA INDEX NAME)

Absolute stereochemistry.

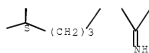
PAGE 1-A



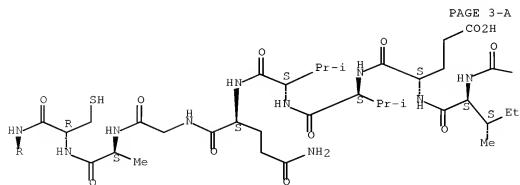
PAGE 1-B



PAGE 2-A

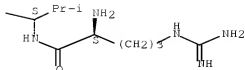


PAGE 2-B



PAGE 3-A

PAGE 3-B



L80 ANSWER 50 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:621243 CAPLUS Full-text

DOCUMENT NUMBER: 121:221243

ORIGINAL REFERENCE NO.: 121:40009a,40012a

TITLE: Limiting dilution analysis of a novel tripeptide anticancer agent Ambamustine (PTT-119): effect on K-562, CCRF-SB and multidrug resistant LoVo-DX cell lines

AUTHOR(S): Manna, Annunziata; Porcellini, Adolfo; Visani, Giuseppe; Marchetti-Rossi, Maria Teresa; Tura, Sante Sez. Ematol., Cent. Trapianto Midollo Osseo, Cremona, 26100, Italy

SOURCE: Experimental Hematology (New York, NY, United States) (1994), 22(6), 517-20
CODEN: EXHMA6; ISSN: 0301-472X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cell suspensions of normal human bone marrow were mixed with human acute lymphoblastic or myelogenous leukemic cells of the CCRF-SB or K-562 lines. After incubating the cell mixts. in vitro with different dose levels of Ambamustine (PTT-119), a quantity of 104 treated cells were dispensed into microculture plates, and graded cell nos. of the lines used to contaminate the normal marrow were added. Limiting dilution anal. (LDA) was used to estimate the frequency of leukemic cells persisting after treatment. Incubation with 50 µg/mL of PTT-119 produced a total elimination of K-562 acute myelogenous blasts, whereas nearly 0.17 and 0.27 leukemic cells were still present in the cell mixts. after treatment with 5 and 25 µg/mL, resp. When normal bone marrow was contaminated with CCRF-SB lymphoblastic cells, incubation with either 50 or 25 µg/mL of PTT-119 produced a complete clearing of leukemic cells, whereas with 5 µg/mL the leukemic cells in each well were 0.18. When PTT-119 was incubated with LoVo-DX, a colon cancer cell line which expresses the pleiotropic drug resistance MDR phenotype, virtually complete inhibition of clonogenic colonies was observed with as little as 5 µg/mL. PTT-119 could be used in clin. trials as a non-cross-resistant agent in multidrug protocol.

CC 1-6 (Pharmacology)

IT Neoplasm inhibitors

(limiting dilution anal. of antitumor agent and effect on multidrug resistant cell lines)

IT 83996-50-3, PTT119 85754-59-2, Ambamustine

RL: S&C (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(limiting dilution anal. of antitumor agent and effect on multidrug resistant cell lines)

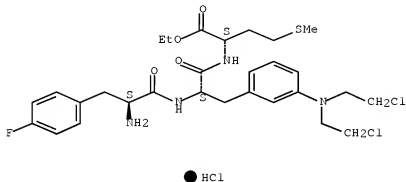
IT 83996-50-3, PTT119 85754-59-2, Ambamustine

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(limiting dilution anal. of antitumor agent and effect on multidrug
resistant cell lines)

RN 83996-50-3 CAPLUS

CN L-Methionine, 4-fluoro-L-phenylalanyl-3-[bis(2-chloroethyl)amino]-L-
phenylalanyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

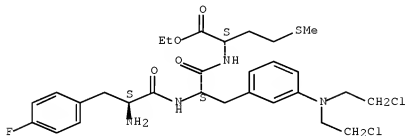
Absolute stereochemistry.



RN 85754-59-2 CAPLUS

CN L-Methionine, 4-fluoro-L-phenylalanyl-3-[bis(2-chloroethyl)amino]-L-
phenylalanyl-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 51 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:622874 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 115:222874

ORIGINAL REFERENCE NO.: 115:37747a,37750a

TITLE: A novel N-myristylated synthetic octapeptide inhibits
protein kinase C activity and partially reverses
murine fibrosarcoma cell resistance to adriamycin
AUTHOR(S): O'Brian, Catherine A.; Ward, Nancy E.; Liskamp, Rob
M.; De Bont, Dries B.; Earnest, Laura E.; Van Boom,
Jacques H.; Fan, Dominic

CORPORATE SOURCE: M.D. Anderson Cancer Cent., Univ. Texas, Houston, TX,
77030, USA

SOURCE: Investigational New Drugs (1991), 9(2),
169-79

CODEN: INNDDK; ISSN: 0167-6997

DOCUMENT TYPE: Journal
 LANGUAGE: English

- AB This report shows that N-acylation of the protein kinase C (PKC) substrate Arg-Lys-Arg-Thr-Leu-Arg-Arg-Leu (RKRTLRLRL) provides it with a potent inhibitory activity against PKC. N-Myristoyl-RKRTLRLRL inhibited Ca^{2+} - and phosphatidylserine (PS)-dependent histone phosphorylation catalyzed by PKC with a 50% inhibitory concentration (IC_{50}) of 5 μM , whereas neither RKRTLRLRL nor myristic acid inhibited PKC-catalyzed histone phosphorylation at concns. as high as 50 μM . A fully active, Ca^{2+} - and PS-independent catalytic fragment of PKC can be generated by limited proteolysis. N-Myristoyl-RKRTLRLRL inhibited histone phosphorylation catalyzed by the catalytic fragment of PKC (IC_{50} = 80 μM), but neither myristic acid nor the nonmyristylated peptide inhibited the activity of the catalytic fragment at concns. up to and including 200 μM . The K_m app and V_{max} app for N-myristoyl-RKRTLRLRL were similar to those of RKRTLRLRL. Thus, N-myristylation provided the octapeptide with an inhibitory activity against PKC but had only minor effects on its K_m app and V_{max} apparatus. Kinetics anal. provided evidence that the peptide inhibited PKC noncompetitively with respect to ATP. The protein kinase inhibitor H7 partially reverses Adriamycin resistance in the multidrug resistant (MDR) murine fibrosarcoma line partially reverses Adriamycin resistance in the Multidrug resistant (MDR) murine fibrosarcoma line UV-2237M-ADRR. N-Myristoyl-RKRTLRLRL also partially reverses Adriamycin resistance in UV-2237M-ADRR cells. These results suggest that potent and selective cell permeable PKC inhibitors may be designed by N-acylating small PKC peptide substrates.
- CC 1-6 (Pharmacology)
- IT Section cross-reference(s): 7
- IT Neoplasms inhibitors
 (fibrosarcoma, adriamycin, resistance to, protein kinase C inhibitor
 myristyl octapeptide reversal of)
- IT 121145-44-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (demethylation of)
- IT 136051-72-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and condensation of, with protected arginylleucine)
- IT 136082-45-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and condensation of, with protected arginyllysinyllarginine)
- IT 136082-44-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and condensation of, with protected pentapeptide)
- IT 136051-71-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and demethylation of)
- IT 136139-95-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and deprotection of)
- IT 136082-46-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and myristylation of)
- IT 136082-43-4
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)

(preparation and protein kinase C-inhibiting activity of, adriamycin resistance reversed by)

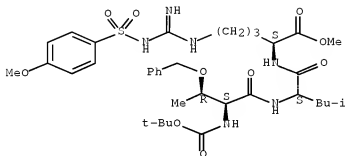
IT 121145-44-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation of)

RN 121145-44-6 CAPLUS

CN L-Ornithine, N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-threonyl]-L-leucyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



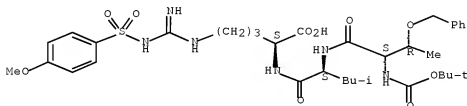
IT 136051-72-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and condensation of, with protected arginylleucine)

RN 136051-72-4 CAPLUS

CN L-Ornithine, N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-threonyl]-L-leucyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 136082-45-6P

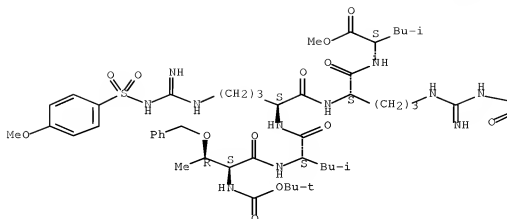
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and condensation of, with protected arginyllysinyllarginine)

RN 136082-45-6 CAPLUS

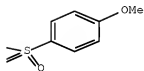
CN L-Leucine, N-[N2-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-threonyl]-L-leucyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 136082-44-5P

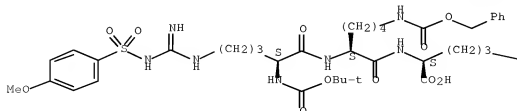
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and condensation of, with protected pentapeptide)

RN 136082-44-5 CAPLUS

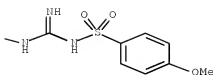
CN L-Ornithine, N2-[N2-[N2-[(1,1-dimethylethoxy)carbonyl]-N-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 136051-71-3P

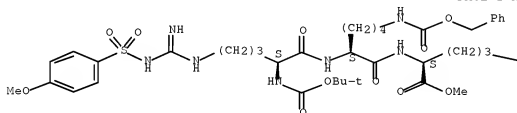
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(Reactant or reagent)
(preparation and demethylation of)

RN 136051-71-3 CAPLUS

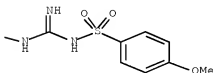
CN L-Ornithine, N2-[N2-[N2-[(1,1-dimethylethoxy)carbonyl]-N-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 136139-95-2P

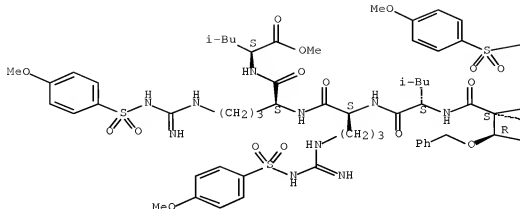
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(Reactant or reagent)
(preparation and deprotection of)

RN 136139-95-2 CAPLUS

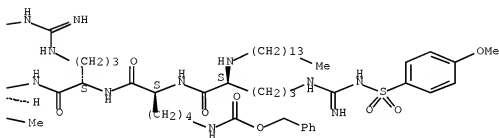
CN L-Leucine, N-[N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-N2-[N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-N2-[N-[N5-[imino[(4-methoxyphenyl)sulfonyl]amino]methyl]-N2-tetradecyl-L-ornithyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-ornithyl]-O-(phenylmethyl)-L-threonyl]-L-leucyl]-L-ornithyl]-L-ornithyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 136082-46-7P

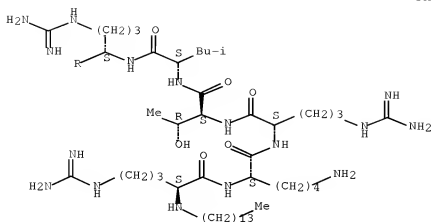
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and myristylation of)

RN 136082-46-7 CAPLUS

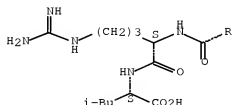
CN L-Leucine, N-[N2-[N-[N-[N2-[N2-[N2-[(1,1-dimethylethoxy)carbonyl]-N5-[imino[[[4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-N5-[imino[[[4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-O-(phenylmethyl)-L-threonyl]-L-leucyl]-N5-[imino[[[4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-N5-[imino[[[4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L80 ANSWER 52 OF 52 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:498409 CAPLUS Full-text

DOCUMENT NUMBER: 103:98409

ORIGINAL REFERENCE NO.: 103:15617a,15620a

TITLE: PTT.119, p-F-Phe-m-bis(2-chloroethyl)amino-L-Phe-Met

ethoxy hydrochloride, a new chemotherapeutic agent

active against drug-resistant tumor cell lines

AUTHOR(S): Yagi, Mary Jane; Chin, Susan E.; Scanlon, Kevin J.;

Holland, James F.; Bekesi, J. George

CORPORATE SOURCE: Cancer Cent., Mount Sinai Sch. Med., New York, NY,

10029, USA

SOURCE: Biochemical Pharmacology (1985), 34(13),

2347-54

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PTT 119 [83996-50-3], a new synthetic tripeptide, was highly effective against the L-phenylalanine mustard (L-PAM) [148-82-3] resistant (L1210/L-PAM and P388/L-PAM) tumor lines, as well as the sensitive L1210 leukemia. Cytolytic activity of PTT 119 against all 3 leukemias was significantly greater than equimolar doses of L-PAM. These in vitro results paralleled the significant increases in mean survival times of hosts and, in some cases, abrogations of tumor formation observed in the in vivo bioassays of PTT 119-treated L1210 and L1210/L-PAM cells. Dose-response studies failed to demonstrate cross-resistance to the tripeptide by L-PAM resistant cells.

Doses of PTT 119 required to reduce the viable fraction by 50% (tissue culture dose 50, TCD50) or 100% (TCD100) were 1.3- to 3-fold lower for the L-PAM resistant cells than for the L1210 leukemia. In comparison, L-PAM was unable to completely eliminate cell survival; 0.2 to 3% of the cells in all 3 leukemias remained viable even at doses of 75 and 163 μM . In similar studies, L1210 leukemia cells made resistant to methotrexate [59-05-2] (L1210 MTX) and cisplatin [15663-27-1] (L1210DDP) were also completely susceptible to PTT 119; TCD50 values of the two resistant lines were 1.94 μM for L1210 MTX and 0.525 μM for L1210DDP compared to 2.38 μM for the susceptible parent L1210S leukemia. Continuous low-dose PTT 119 treatment of MJY- α mammary tumor cells for 8 mo and exposure of L1210 leukemia to escalating levels of tripeptide for over 100 passages failed to select or induce drug-resistant phenotypes in either cell line. PTT 119 appears to be a poor mutagen and is unlikely to readily increase the probability of drug-resistant mutants in the tumor cell populations.

CC 1-6 (Pharmacology)

IT Neoplasms inhibitors

(fluorophenylalanine-bis(chloroethyl)amino-phenylalanine-methionine as, drug resistance in relation to)

IT 83996-50-3

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(neoplasms-inhibiting activity of, drug resistance in relation to)

IT 83996-50-3

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

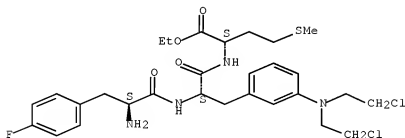
(Biological study); USES (Uses)

(neoplasms-inhibiting activity of, drug resistance in relation to)

RN 83996-50-3 CAPLUS

CN L-Methionine, 4-fluoro-L-phenylalanyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HC1

SEARCH HISTORY

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=> d stat que l41; d his nofile
L7      197142 SEA FILE=CAPLUS ABB=ON ANTITUMOR AGENTS/CT
L8      506787 SEA FILE=CAPLUS ABB=ON NEOPLAS?/CW
L9      866071 SEA FILE=CAPLUS ABB=ON RESISTAN?/OBI
L11     36803 SEA FILE=CAPLUS ABB=ON DRUG RESISTANCE/CT
L12     17430 SEA FILE=CAPLUS ABB=ON (L7 OR L8) AND L11
L13     20417 SEA FILE=CAPLUS ABB=ON (L7 OR L8)(L)L9
L14     23359 SEA FILE=CAPLUS ABB=ON (L12 OR L13)
L15     SEL L14 1- RN : 50661 TERMS (TERM LIMIT EXCEEDED)
L16     50660 SEA FILE=REGISTRY ABB=ON L15
L17     SEL L14 6853- RN : 53251 TERMS (TERM LIMIT EXCEEDED)
L18     53251 SEA FILE=REGISTRY ABB=ON L17
L19     SEL L14 10674- RN : 35492 TERMS
L20     35492 SEA FILE=REGISTRY ABB=ON L19
L21     268 SEA FILE=CAPLUS ABB=ON ANTIMICROTUB?/OBI
L22     23854 SEA FILE=CAPLUS ABB=ON MICROTUBULE#/OBI
L23     8827 SEA FILE=CAPLUS ABB=ON MULTIDRUG RESISTANCE/CT
L24     6362 SEA FILE=CAPLUS ABB=ON (L21 OR L22 OR L23) AND (L7 OR L8)
L25     3175 SEA FILE=CAPLUS ABB=ON L24 NOT L14
L26     SEL L25 1- RN : 52585 TERMS (TERM LIMIT EXCEEDED)
L27     52585 SEA FILE=REGISTRY ABB=ON L26
L28     SEL L25 991- RN : 50779 TERMS (TERM LIMIT EXCEEDED)
L29     50779 SEA FILE=REGISTRY ABB=ON L28
L30     SEL L25 1660- RN : 41595 TERMS
L31     41595 SEA FILE=REGISTRY ABB=ON L30
L32     254797 SEA FILE=REGISTRY ABB=ON (L16 OR L18 OR L20 OR L27 OR L29 OR
L38     L31)
STR
```



```
VAR G1=O/S/N
NODE ATTRIBUTES:
NSPEC   IS RC      AT    1
NSPEC   IS RC      AT    2
CONNECT IS E3 RC AT    5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
```

```
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13
```

```
STEREO ATTRIBUTES: NONE
L41      11974 SEA FILE=REGISTRY SUB=L32 SSS FUL L38
```

```
100.0% PROCESSED 13031 ITERATIONS
SEARCH TIME: 00.00.02
```

11974 ANSWERS

FILE 'CAPLUS' ENTERED AT 10:49:10 ON 08 SEP 2008

E US2003-666722/APPS

L1 1 SEA ABB=ON US2003-666722/AP
D SCAN
SEL RN

FILE 'REGISTRY' ENTERED AT 10:49:45 ON 08 SEP 2008

L2 566 SEA ABB=ON (100-66-3/BI OR 100564-78-1/BI OR 104-87-0/BI OR
104-88-1/BI OR 107905-52-2/BI OR 111-87-5/BI OR 1121-57-9/BI
OR 112898-23-4/BI OR 114-76-1/BI OR 114977-28-5/BI OR 120944-75
-4/BI OR 127106-02-9/BI OR 128437-36-5/BI OR 128437-66-1/BI OR
128437-74-1/BI OR 13139-15-6/BI OR 13734-34-4/BI OR 13781-71-0/
BI OR 138802-17-2/BI OR 145432-51-5/BI OR 151-10-0/BI OR
151-18-8/BI OR 15504-41-3/BI OR 156-06-9/BI OR 160785-01-3/BI
OR 161479-50-1/BI OR 167158-86-3/BI OR 169181-24-2/BI OR
184434-18-2/BI OR 184434-19-3/BI OR 18962-05-5/BI OR 207910-81-
4/BI OR 207910-88-1/BI OR 207910-90-5/BI OR 208521-14-6/BI OR
213206-68-9/BI OR 21744-88-7/BI OR 2280-27-5/BI OR 228266-38-4/
BI OR 228266-40-8/BI OR 228266-42-0/BI OR 228266-48-6/BI OR
228266-49-7/BI OR 23082-30-6/BI OR 25080-84-6/BI OR 2605-67-6/B
I OR 26269-45-4/BI OR 3132-99-8/BI OR 328-51-8/BI OR 3282-30-2/
BI OR 33069-62-4/BI OR 3541-37-5/BI OR 40447-58-3/BI OR
4530-20-5/BI OR 456-48-4/BI OR 461-72-3/BI OR 498-62-4/BI OR
500229-32-3/BI OR 500229-47-0/BI OR 529-20-4/BI OR 5381-20-4/BI
OR 540-51-2/BI OR 543-24-8/BI OR 55447-00-2/BI OR 556-82-1/BI
OR 564441-48-1/BI OR 564441-50-5/BI OR 57-22-7/BI OR 5717-37-3/
BI OR 5779-95-3/BI OR 587-04-2/BI OR 591-31-1/BI OR 5973-71-7/B
I OR 59752-74-8/BI OR 610786-69-1/BI OR 610786-70-4/BI OR
61676-25-3/BI OR 620-23-5/BI OR 628-21-7/BI OR 628-77-3/BI OR
630424-73-6/BI OR 636-72-6/BI OR 64-04-0/BI OR 64263-80-5/BI
OR 66386-16-1/BI OR 676626-71-4/BI OR 676626-79-2/BI OR
676626-83-8/BI OR 676626-85-0/BI OR 676626-89-4/BI OR 676626-91
-8/BI OR 676626-93-0/BI OR 676626-95-2/BI OR 676626-97-4/BI OR
676626-99-6/BI OR 676627-01-3/BI OR 676627-02-4/BI OR 676627-05
-7/BI OR 676627-06-8/BI OR 676627-09-1/BI OR 676627-11-5/BI OR
676627-13-7/BI OR 676627-15-9/BI OR 676627-17-1/BI OR 676627-18
-2/BI OR 676627-20-6/BI OR 676627-21-7/BI OR 676627-23-9/BI OR
676627-25-1/BI OR 676627-27-3/BI OR 676627-31-9/BI OR 676627-33
-1/BI OR 676627-35-3/BI OR 676627-37-5/BI OR 676627-39-7/BI OR
676627-42-2/BI OR 676627-44-4/BI OR 676627-46-6/BI OR 676627-48
-8

L3 5 SEA ABB=ON C28H45N3O5/MF AND L2
D SCAN

L4 2 SEA ABB=ON "L-VALINAMIDE, N,O,B,H-TETRAMETHYL-L-TYROSYL-N-((1S,
SYL-N-((1S,2E)-3-CARBOXY-1-(1-METHYLETHYL)-2-BUTENYL)-N,3-DIMET
HYL"*/CN

D SCAN

STR

L6 50 SEA SSS SAM L5

FILE 'CAPLUS' ENTERED AT 11:03:23 ON 08 SEP 2008

L7 197142 SEA ABB=ON ANTITUMOR AGENTS/CT

L8 506787 SEA ABB=ON NEOPLAS*/CW

L9 866071 SEA ABB=ON RESISTAN*/OBI

L10 28344 SEA ABB=ON (L7 OR L8) AND L9

D SCAN L1

L11 36803 SEA ABB=ON DRUG RESISTANCE/CT

L12 17430 SEA ABB=ON (L7 OR L8) AND L11

L13 20417 SEA ABB=ON (L7 OR L8) (L) L9
 L14 23359 SEA ABB=ON (L12 OR L13)

 FILE 'REGISTRY' ENTERED AT 11:35:00 ON 08 SEP 2008

 FILE 'CAPLUS' ENTERED AT 11:35:00 ON 08 SEP 2008
 SET SMARTSELECT ON
 L15 SEL L14 1- RN : 50661 TERMS (TERM LIMIT EXCEEDED)
 SET SMARTSELECT OFF

 FILE 'REGISTRY' ENTERED AT 11:37:26 ON 08 SEP 2008
 L16 50660 SEA ABB=ON L15

 FILE 'CAPLUS' ENTERED AT 11:39:41 ON 08 SEP 2008
 SET SMARTSELECT ON
 L17 SEL L14 6853- RN : 53251 TERMS (TERM LIMIT EXCEEDED)
 SET SMARTSELECT OFF

 FILE 'REGISTRY' ENTERED AT 11:41:09 ON 08 SEP 2008
 L18 53251 SEA ABB=ON L17

 FILE 'CAPLUS' ENTERED AT 11:43:33 ON 08 SEP 2008
 SET SMARTSELECT ON
 L19 SEL L14 10674- RN : 35492 TERMS
 SET SMARTSELECT OFF

 FILE 'REGISTRY' ENTERED AT 11:47:03 ON 08 SEP 2008
 L20 35492 SEA ABB=ON L19

 FILE 'STNGUIDE' ENTERED AT 11:53:32 ON 08 SEP 2008

 FILE 'CAPLUS' ENTERED AT 11:59:21 ON 08 SEP 2008
 L21 268 SEA ABB=ON ANTIMICROTUB#/OBI
 E MICROTUB
 L22 23854 SEA ABB=ON MICROTUBULE#/OBI
 E DRUG RESISTANCE+ALL/CT
 L23 8827 SEA ABB=ON MULTIDRUG RESISTANCE/CT
 L24 6362 SEA ABB=ON (L21 OR L22 OR L23) AND (L7 OR L8)
 L25 3175 SEA ABB=ON L24 NOT L14
 D COST

 FILE 'REGISTRY' ENTERED AT 12:02:11 ON 08 SEP 2008

 FILE 'CAPLUS' ENTERED AT 12:02:20 ON 08 SEP 2008
 SET SMARTSELECT ON
 L26 SEL L25 1- RN : 52585 TERMS (TERM LIMIT EXCEEDED)
 SET SMARTSELECT OFF

 FILE 'REGISTRY' ENTERED AT 12:03:23 ON 08 SEP 2008
 L27 52585 SEA ABB=ON L26

 FILE 'CAPLUS' ENTERED AT 12:05:35 ON 08 SEP 2008
 SET SMARTSELECT ON
 L28 SEL L25 991- RN : 50779 TERMS (TERM LIMIT EXCEEDED)
 SET SMARTSELECT OFF

 FILE 'REGISTRY' ENTERED AT 12:06:15 ON 08 SEP 2008
 L29 50779 SEA ABB=ON L28

 FILE 'CAPLUS' ENTERED AT 12:08:21 ON 08 SEP 2008

L30 SET SMARTSELECT ON
 SEL L25 1660- RN : 41595 TERMS
 SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 12:09:06 ON 08 SEP 2008

L31 41595 SEA ABB=ON L30
 L32 254797 SEA ABB=ON (L16 OR L18 OR L20 OR L27 OR L29 OR L31)
 D QUE L5
 L33 50 SEA SUB=L32 SSS SAM L5
 L34 13031 SEA SUB=L32 SSS FUL L5 EXTEND
 L35 11596 SEA SUB=L32 SSS FUL L5
 SAVE TEMP L35 BET/22FULL/A
 L36 0 SEA ABB=ON L4 AND L35
 D QUE L4
 L37 2 SEA ABB=ON L4 AND L32
 L38 STR L5
 L39 50 SEA SUB=L32 SSS SAM L38
 L40 13031 SEA SUB=L32 SSS FUL L38 EXTEND
 L41 11974 SEA SUB=L32 SSS FUL L38
 SAVE TEMP L41 BET/22FULL/A
 L42 2 SEA ABB=ON L41 AND L4
 L43 1 SEA ABB=ON 57-22-7
 L44 1 SEA ABB=ON 865-21-4
 L45 1 SEA ABB=ON 33069-62-4
 L46 1 SEA ABB=ON 71486-22-1
 L47 1 SEA ABB=ON 114977-28-5
 L48 5 SEA ABB=ON (L43 OR L44 OR L45 OR L46 OR L47)
 D SCAN

FILE 'CAPLUS' ENTERED AT 12:20:02 ON 08 SEP 2008

L49 56194 SEA ABB=ON L41
 L50 2 SEA ABB=ON L4
 L51 28149 SEA ABB=ON L48
 L52 1009 SEA ABB=ON L49 AND L51
 L53 15262 SEA ABB=ON L49(L) (THU OR BAC OR PAC OR PKT OR DMA)/RL
 L54 799 SEA ABB=ON L53 AND L51
 L55 3565 SEA ABB=ON (L7 OR L8) AND L53
 L56 294 SEA ABB=ON L55 AND (L23 OR L11 OR L9)
 L57 87 SEA ABB=ON L55 AND (L23 OR L11 OR L9) AND L51
 L58 20 SEA ABB=ON L55 AND (L23 OR L11 OR L9) AND (L21 OR L22)
 D SCAN TI
 L59 2420596 SEA ABB=ON PHARMAC?/SC,SX
 L60 18 SEA ABB=ON L58 AND L59
 L61 2 SEA ABB=ON L58 NOT L60
 D SCAN TI HITIND
 D QUE NOS L60
 L62 3016 SEA ABB=ON L9(L) L51
 L63 3565 SEA ABB=ON L53 AND (L7 OR L8)
 L64 21 SEA ABB=ON L53 AND (L7 OR L8) AND L62
 L65 192 SEA ABB=ON L53(L) L9
 L66 106 SEA ABB=ON L65 AND (L7 OR L8)
 D QUE NOS
 L67 106 SEA ABB=ON (L66 AND (L11 OR L23)) OR (L66 AND L9(L) (L7 OR L8))
 L68 74 SEA ABB=ON (L66 AND (L11 OR L23))
 L69 11026 SEA ABB=ON L49 AND PATENT/DT
 L70 2126 SEA ABB=ON L49 AND REVIEW/DT
 L71 45168 SEA ABB=ON L49 NOT L69
 L72 36455 SEA ABB=ON L71 AND PY<2003
 L73 6492 SEA ABB=ON L69 AND (PD<20020920 OR AD<20020920 OR PRD<20020920)


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    )
L74      43625 SEA ABB=ON (L70 OR L72 OR L73)
L75      106 SEA ABB=ON L53 AND L66
L76      45 SEA ABB=ON L74 AND L66
L77      73 SEA ABB=ON (L60 OR L64 OR L76)
L78      52 SEA ABB=ON (L60 OR L64 OR L66) AND L74

FILE 'REGISTRY' ENTERED AT 12:33:44 ON 08 SEP 2008
D QUE L4

FILE 'CAPLUS' ENTERED AT 12:33:52 ON 08 SEP 2008
D QUE NOS L50
D IBIB ABS HITSTR L50

FILE 'REGISTRY' ENTERED AT 12:34:24 ON 08 SEP 2008
D STAT QUE L41

FILE 'CAPLUS' ENTERED AT 12:34:35 ON 08 SEP 2008
D QUE NOS L60
D QUE NOS L64
D QUE NOS L66
D QUE NOS L74
L79      52 SEA ABB=ON L74 AND (L60 OR L64 OR L66) NOT L50
D IBIB ABS HITSTR L50 2

FILE 'REGISTRY' ENTERED AT 12:36:21 ON 08 SEP 2008
D IDE L48 1-5

FILE 'CAPLUS' ENTERED AT 12:36:37 ON 08 SEP 2008
D QUE NOS L60
D QUE NOS L64
D QUE NOS L66
D QUE NOS L74
L80      52 SEA ABB=ON L74 AND (L60 OR L64 OR L66) NOT L50
D IBIB ABS HITIND HITSTR L80 1-52

FILE 'HOME' ENTERED AT 12:38:11 ON 08 SEP 2008
D STAT QUE L41

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